IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LIGITATION	**Master File No. 2:12-MD-02327** **MDL No. 2327**
THIS DOCUMENT RELATES TO PLAINTIFFS: **Wave 1 Cases**	**JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

RULE 26 EXPERT REPORT OF DANIEL ELLIOTT, M.D.

I. BACKGROUNDS AND QUALIFICATIONS

I am an Associate Professor of Urology, section of Female Urology and Reconstructive Surgery, at Mayo Clinic Graduate School of Medicine in Rochester, Minnesota. My current curriculum vita, attached hereto as Exhibit "A", more fully and accurately reflects my training, background, academic activity and publications. However, briefly, I received an M.D. in 1993 from Loma Linda University School of Medicine in Loma Linda, California. Following graduation from medical school, I completed one year of General Surgery and five years of Surgical Urology residency at the Mayo Graduate School of Medicine at the Mayo Clinic in 1999. I then completed a one-year advanced surgical fellowship at Baylor College of Medicine in Houston, Texas, in Neurourology, Urodynamics and Voiding Dysfunction. I then re-joined the faculty at the Mayo Clinic, where I have spent the last fifteen years specializing in treating pelvic organ prolapse and urinary incontinence in women and urinary incontinence in men. I have published nearly 60 peer-reviewed articles and given over 100 lectures nationally and internationally pertaining to urinary incontinence and pelvic organ prolapse. I have specifically authored two published scientific manuscripts dealing with polypropylene meshes in the animal model. A Mayo Clinic colleague and I were the first to perform robotic sacrocolpopexy surgery for the treatment of high-grade prolapse and to publish extensively on the subject and the first to perform and publish on the outpatient, non-mesh transobturator sling.

During my training, I was introduced to the use of synthetic midurethral slings for incontinence repair. I have used the Mentor OB/Tape products as well as mesh slings made by AMS and Coloplast. As of over a year ago, I decided to no longer use meshes in my practice through the transvaginal route unless there is absolutely no other alternative. The reason that I made this decision is that my practice has become increasingly dedicated to treating a host of life-altering complications associated with the use of both SUI and POP meshes, including

meshes made by Ethicon. Neither I, nor my colleagues at Mayo, have ever used transvaginal POP kits as we felt that the risk to patients was too great. Having treated hundreds of patients with mesh-related complications (both SUI and POP), I feel that we made the right decision not to include them as part of our treatment regimen. I only use mesh for POP repair through robotic sacrocolpopexy, as it is not a transvaginal surgery, uses much less mesh, and is associated with significantly less complications than transvaginal mesh prolapse repair.

I am a frequent invited national and international lecturer at medical and surgical conferences addressing stress urinary incontinence and pelvic organ prolapse, their evaluation, treatment, surgical options and management of complications. I have taken and passed the subspecialty credentialing process recently established by the combined boards of the American Board of Urology and American Board of Obstetrics and Gynecology in Female Pelvic Medicine and Reconstructive Surgery.

II. BASIS OF OPINIONS

I have been asked to provide opinions regarding the subject of pelvic organ prolapse, its evaluation, treatments, surgical options and management of complications as well as to address the actions of Ethicon, Inc., Ethicon Women's Health and Urology, a Division of Ethicon, Inc., Gynecare and Johnson & Johnson (collectively referred to as Ethicon), regarding its transvaginal mesh pelvic floor repair products for prolapse. The focus of my investigation for this report is on the GYNECARE PROLIFT Total, Anterior, and Posterior Pelvic Floor Repair Systems (collectively referred to as "Prolift" or the "Prolift System"). My opinions are based on my personal knowledge, experience, and my investigation in this case. All of my opinions, and the basis of these opinions, are true and correct to the best of my knowledge and belief, including those related to scientific and medical issues, which I believe are true and correct to a reasonable degree of scientific and medical probability. I do, however, reserve the right to supplement this report and my opinions in light of any additional material or information provided to me, including any reports submitted and/or any other discovery that is taken in this case. Furthermore, if called to testify, I would plan to use various demonstrative exhibits, animations, video recordings, and/or anatomic models to show the relevant anatomy and surgical procedures and to describe my opinions as set forth in this report. The materials I have reviewed and relied upon to form my opinions for this report are attached as Exhibit "B".

III. SUMMARY OF OPINIONS

A. Lack of Clinical Benefit

1. Overall, patients implanted with non-absorbable, transvaginal synthetic mesh for pelvic organ prolapse, including the Prolift System, do not have demonstrable improvement in symptomatic results over traditional, non-mesh repair.

2. Overall, patients implanted with non-absorbable, transvaginal synthetic mesh for pelvic organ prolapse, including the Prolift System, have demonstrably worse improvement in their quality of life (QOL) over traditional, non-mesh repair.

3. Overall, patients implanted with non-absorbable, transvaginal synthetic mesh for pelvic organ prolapse, including the Prolift System, do not have demonstrable improvement in reoperation rates over traditional, non-mesh repair.

4. The increased patient risks, complication rates, and the added expense of the Prolift System far outweigh any stated or implied benefits.

5. There was no need for the Prolift System, a non-absorbable, synthetic mesh, to be sold and marketed as a surgical treatment and procedure for pelvic organ prolapse (POP) as there were safe, effective and reasonable alternative surgical treatments available at the time this product was launched that did not needlessly endanger patients nor carry the likelihood or risk of serious injury that has been associated with the Prolift System. Accordingly, the Prolift System should have never been marketed to surgeons or patients in the first place, and I agree with Ethicon's 2012 decision to cease marketing the Prolift System for use in the United States.

B. Complication Rate

1. Synthetic transvaginal meshes for POP, including the Prolift System, subject patients to needless danger through increased risks not present in traditional, non- mesh surgery for POP repair. Prolift has, therefore, caused serious and potentially permanent injuries due to complications associated with its implantation for POP repair.

2. Even when surgeons used the Prolift System as designed and marketed, it was unsafe to patients for its intended use as a method of surgical POP repair because of patient-to-patient anatomic variability and surgeon-to-surgeon variability in experience, training and technique, as well as the inherently unsafe characteristics of the procedure and mesh.

3. Because non-absorbable, synthetic, polypropylene mesh such as Prolift causes an intense foreign body reaction in pelvic tissue, there is no way to safely implant these products into a woman's pelvic tissue without an increased risk of serious complications including, but not limited to, pain associated with the implant procedure (including but not limited to nerve, vascular, organ and tissue damage), chronic pelvic pain associated with fibrosis and scarring, adhesions, vaginal retraction and shortening, fistula formation, granuloma formation, chronic infection associated with, among other things, the product's implantation into a clean/contaminated field and the intense inflammatory response to the polypropylene, chronic wound healing issues, organ erosion, vaginal extrusion/exposure, chronic pelvic pain associated with the explant procedure (including but not limited to nerve, vascular, organ and tissue damage) , de novo incontinence, significant dyspareunia (painful intercourse), and the lack of a safe and effective method to treat the complications, including the removal of the mesh when necessary.

C. Data Withheld From Physicians

1. Ethicon failed to completely disclose to physicians and their patients the known risks of prolapse surgery using Prolift. By withholding this information and failing to provide adequate warnings and/or instructions, Ethicon failed to act as a reasonably prudent medical device manufacturer. Because of its actions, Ethicon knowingly exposed patients to needless, preventable danger, harm and permanent suffering. Ethicon's failure to disclose risks known to it about the Prolift took away physicians' ability to properly and appropriately consent their patients.

2. Ethicon failed to disclose the lack of benefit of POP surgery using the Prolift System to physicians and patients. By withholding this information and failing to provide adequate warnings and/or instructions, Ethicon failed to act as a reasonably prudent medical device manufacturer and thereby exposed patients to needless danger and harm.

3. Ethicon inadequately informed physicians and their patients that the Prolift System caused significant risks to normal sexual activity. Specifically, Ethicon made a conscious decision not to include statements regarding the likelihood that undergoing a POP surgery utilizing the Prolift System could cause "pain with intercourse and pelvic pain," and because of these misrepresentations, countless women will permanently and needlessly be forced to suffer lifelong pain and embarrassment.

D. Breach of Duty by Ethicon

1. Ethicon breached its duty of reasonable care to implanting surgeons and to patients by marketing and selling Prolift Pelvic Floor Repair Systems as a "revolutionary" surgical device ***and*** procedure without sufficient evidence to support the Prolift System's safety, effectiveness and benefit, and with specific knowledge of the increased risks of non-absorbable, synthetic surgical mesh for POP, including its product, Prolift.

2. Ethicon breached its duty of reasonable care to implanting surgeons and to patients by marketing and selling the Prolift System (both the product *and* the procedure) to surgeons and patients without proper warnings, proper training, without proper instructions for use and without sufficient evidence of its safety and efficacy, thereby exposing patients to needless danger and unreasonable risk of harm.

3. Ethicon breached its duty of reasonable care to implanting surgeons and to patients by failing to timely disclose its knowledge of a significant increase in complications associated with the Prolift System even though it had the ability to do so through physician communications, "*Dear Surgeon*" letters, its sales force, sales and marketing brochures to physicians and patients and/or updates to its Instructions for Use to physicians, and in fact used those means of communications to minimize the impact of risk information when it was brought to light through other sources.

IV. NORMAL ANATOMY AND PELVIC ORGAN PROLAPSE

The normal vagina is a functional, pliable, distensible, mobile, and well-supported structure. Pelvic organ prolapse (POP) is a condition in which one or more of the female pelvic organs (bladder, rectum, uterus, and/or intestines) drop into the vagina to varying degrees, as a result of weakened vaginal tissue to form a bulge or fullness in the vagina. POP can affect the quality of life (QOL) of women; however, POP is not a life-threatening condition. POP is for many women a normal part of the aging process and can result from some combination of increasing age, multiple childbirths, frequent heavy lifting, chronic cough, obesity, constipation, previous hysterectomy and genetic predisposition. Symptoms of POP are usually limited to QOL issues such as the sensation of pelvic fullness, pressure and interference with sexual activity. It can also impact on urination and bowel function. POP is a relatively common condition, with up to 50% of women who have had children having some degree of POP; however, only a fraction of those women are symptomatic. Medical device manufacturers such as the manufacturer of the Prolift, Ethicon, perceived that the potential surgical market created a desirable target for device manufacturers eager to capture market share. (Wall L: The perils of commercially driven surgical innovation. Am J of Obstetrics and Gyne Jan 2010; 202.30e1-4).

As mentioned above, POP is a protrusion or a falling down of one or more of the pelvic organs into the vagina. This can affect one or more of the vaginal "compartments." These compartments are:

1. The bladder (called an Anterior Compartment Prolapse or Cystocele).
2. The rectum (called the Posterior Compartment Prolapse or Rectocele).
3. The uterus (called Uterine Prolapse).
4. The small intestines (called the Apical Compartment Prolapse or Enterocele).
5. In cases where POP affects all of the compartments, this is often referred to as a Vaginal Vault Prolapse.

Treatment for female pelvic organ prolapse can be generally broken down into four main categories:

1. Behavior modification & Pelvic Floor Therapy & Exercises
2. Medication
3. Pessary
4. Surgical treatment

V. TREATMENT

A. Traditional POP Treatment Options

There are multiple well-established treatment options for treating POP. A thorough understanding of the risks and benefits of each of the POP treatment options is imperative for the treating physician to evaluate and recommend appropriate therapy for each patient since each patient represents unique characteristics, symptoms, and risk factors, which can affect the success and complications of any therapy. Following a thorough physical exam by a trained

medical practitioner, the severity and QOL impact of the POP is determined. Management options of POP can be broken down into several broad categories such as observation, behavioral therapies, pelvic floor exercises, pessary use, and, as a last resort, surgery. Since POP is primarily a QOL issue, the physician must first determine whether or not the POP is actually problematic for the patient. Many times the POP is mild and causes either no or only minimal symptoms. In this frequent situation, the safest treatment option is observation with periodic reevaluation to determine if the POP and the patient's symptoms progress or not. For the patient with POP that is symptomatic, further conservative options can be considered such as behavioral changes (weight loss, lifestyle changes), pelvic floor exercises and/or the use of pessary devices.

Surgical procedures should usually be reserved for severe, high grade POP that is negatively impacting the QOL for the woman. Surgical repair of POP has been documented and has evolved over the years. Traditional surgery is performed from either the vagina (termed "transvaginal") or from the abdomen (termed "transabdominal"), with the latter group being performed either with an abdominal incision (Abdominal Sacrocolpopexy) or with minimally-invasive procedures such as with laparoscopic or robotic technology. The Prolift procedure was developed as an alternative procedure to the traditional methods of treating prolapse. By definition, a comparison of the safety and effectiveness/risks and benefits of the Prolift with the alternatives requires a comparison with these traditional procedures.

B. Traditional, Transvaginal NON-Mesh POP Procedures

Traditional transvaginal surgery for POP utilizes an incision through the wall of the vagina hence the term "transvaginal" literally meaning "through the vagina." It is imperative to recognize the basic difference between transvaginal and transabdominal (through the abdomen) surgery since the surgical route chosen affects success, complications, and QOL results.

Traditional non-mesh transvaginal surgery relies on the mobilization and the stitching together of the patient's own deep vaginal tissues (also known as "native tissue") to support the vagina and to repair the POP. Traditional transvaginal surgery for POP, in contrast to Prolift Pelvic Floor Repair Systems, does NOT utilize the blind passage of trocars or mesh in its repair.

One of the most significant arguments used by mesh manufacturers to justify vaginal mesh use over the traditional, non-mesh POP repairs was the misconceived notion that traditional repairs had failure rates of up to 30-40%. This failure rate was based primarily on the work of the 2001 National Institutes of Health (NIH) Workshop on Standardization of Terminology for Researchers in Pelvic Floor Disorders. However, since the Workshop's recommendations in 2001, there have been significant advancements in the understanding of what is normal vaginal support, pelvic prolapse, POP symptoms, and the very critical issue of what patients perceive as a successful outcome following POP surgery. What is now apparent is that the NIH POP Workshop grading system was so strict that a large percentage of average healthy women would fail if graded under that system. This misconception has now been recognized in the medical literature. Currently, within contemporary POP studies which utilize up-to-date prolapse

definitions, the accepted failure rate of traditional, non-mesh POP repairs is less than 15% and closer to 12%.[1] [2] [3]

C. Transabdominal/Laparoscopic/Robotic POP Repair

Sacrocolpopexy is a procedure performed through the abdomen. Although not without risk, sacrocolpopexy is superior to transvaginal mesh procedures as it offers a greater chance of long-term anatomical and symptomatic POP success, with fewer risks. Traditionally, this approach utilized an incision in the lower abdomen. However, with the advancement of minimally invasive procedures such as laparoscopy and robotic surgery, the procedure is increasingly performed using these less invasive alternatives. The procedure entails stitching a mesh or biomaterial to the top, apex and bottom of the vagina then stitching that same mesh or biomaterial to the large bones at the base of the spine called the sacrum.

D. History of Synthetic Mesh

Abdominal and thoracic wall weaknesses, called hernias, exist due to inherent weaknesses within the abdominal wall or thoracic wall due to conditions such as birth defects, surgery, and radiation effects. Traditional hernia repair surgery evolved using sutures (stitches) to bring the native tissue together. However, due to the inherent weaknesses of the tissues, failure was common and frequently resulted in significant pain and suffering for the patient. Therefore, in the 1950's, surgical meshes for hernia repairs were introduced. Subsequently, academic presentations, surgical reports and journal manuscripts began to describe mesh-related complications such as chronic pain, abdominal wall rigidity, mesh contraction, infection, fistula formation, recurrence and chronic inflammatory process.[4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [14] [15] [16] [17] [18] [19] [20] [21] [22]

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[1] Weber AM, Walters MD, Peidmonte MR et al: Anterior Colporraphy: A randomized trial of three surgical techniques. Am J Obstet Gynecol (2001) 185(6):1299-304; discussions 1304-6. 172

[2] Weber AM, Abrams P, Brubaker L: The standardization of terminology for researchers in female pelvic floor disorders. Int Urogynecol J (2001) 12:178-186

[3] Chmielewski L, Walters MD, Weber AM, et al: Reanalysis of a randomized trial. J ObstetGynecol (2011) 205:96.e1-8

[4] Klosterhalfen B, Junge K, Klinge W. The lightweight and large porous mesh concepts for hernia repair. Expert Rev Med Devices. 2005 Jan;2(1):103-17.

[5] Agresta F, Baldazzi G, Ciardo et al: Lightweight partially absorbable monofilament mesh (polyproylene/poliglecaprone 25) for TAPP inguinal hernia repair. Surg laparosc endosc percutan tech 2007, 17;91-94.

[6] Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia (1997) 1:15-21.

[7] Bellon J, Honduvilla N, Jurado F et al: In vitro interaction of bacteria with polypropylene/ePTFE prostheses. Biomaterials. 2001 Jul;22(14):2021-4.

[8] Bouikerrou M, Boulanger L, Rubod C et al: Study of the biomechanical properties of synthetic implanted in vivo. European J. Obstet & Gynecol and Repro Bio 134: (2007)262-267.

[9] Klinge U, Klosterhalfen M, Muller A et al: Shrinking of polypropylene mesh in vivo: an experiment study in dogs. European Journal of Surgery Volume 164, Issue 12, pages 965–969, December 1998.

[10] Klinge U, Klosterhalfen B, Muller M et al: Foreign body reaction to meshes used for the repair of abdominal wall hernias. Eur J Surg. 1999 Jul;165(7):665-73.

[11] Klinge U, Klosterhalfen B, Birkenhauer V: Impact of polymer pore size on the interface scar formation in a rat model. J. Surgical Research 103, 208-214 (2002).

An abundant amount of evidence in the medical literature and basic science data has been gathered over the past two decades that indicates that there is a strong and direct relationship between postoperative mesh complications and mesh design.[23 24 25 26 27 28 29 30 31 32 33]. Reducing mesh-related complications demands a thorough understanding and knowledge of the chemical, physical and synthetic characteristics of meshes and how they react inside the human body. Based upon vast amounts of general surgery and basic science literature, there is a consensus that synthetic meshes that are lower weight (less surface area), larger pore size, higher porosity, monofilament, and that are capable of maintaining their elasticity and structural stability during and after implantation will have better results with fewer complications. Of all the mesh characteristics, pore size and stability of the mesh are among the most important.

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[16] Cappelletti M, Attolini G, Cangioni G, et al. The use of mesh in abdominal wall defects.Minerva Chir. 1997 Oct;52(10):1169-76.

[17] Klosterhalfen B, Klinge W, Hermanns B et al: Pathology of traditional surgical nets for hernia repair after long-term implantation in humans. [ABSTRACT] Chirugr 2000;71:43-51.

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[23] ETH.MESH.00869977 – 00870098

[24] ETH.MESH.02589033 – 02589079

[25] Robinson deposition 3-13; pg 126-130.

[26] Klosterhalfen B, Junge K, Klinge W. The lightweight and large porous mesh concepts for hernia repair. Expert Rev Med Devices. 2005 Jan;2(1):103-17.

[27]Agresta F, Baldazzi G, Ciardo et al: Lightweight partially absorbable monofilament mesh (polyproylene/poliglecaprone 25) for TAPP inguinal hernia repair. Surg laparosc endosc percutan tech 2007, 17;91-94.

[28] Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia (1997) 1:15-21.

[29] Bellon J, Honduvilla N, Jurado F et al: In vitro interaction of bacteria with polypropylene/ePTFE prostheses. Biomaterials. 2001 Jul;22(14):2021-4.

[30] Bouikerrou M, Boulanger L, Rubod C et al: Study of the biomechanical properties of synthetic implanted in vivo. European J. Obstet & Gynecol and Repro Bio 134: (2007)262-267.

[31] Klinge U, Klosterhalfen M, Muller A et al: Shrinking of polypropylene mesh in vivo: an experiment study in dogs. European Journal of Surgery Volume 164, Issue 12, pages 965–969, December 1998.

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[33] Klinge U, Klosterhalfen B, Birkenhauer V: Impact of polymer pore size on the interface scar formation in a rat model. J. Surgical Research 103, 208-214 (2002).

E. Synthetic Mesh Use in Urogynecology

1. Sacrocolpopexy

Synthetic meshes are used transabdominally in sacrocolpopexy. Sacrocolpopexy can now be performed using laparoscopic and robotic technologies. Although mesh is used in sacrocolpopexy, there are important distinctions between the two procedures. As explained above, the mesh used in sacrocolpopexy is inserted through the sterilized transabdominal approach whereas in the transvaginal procedure, the mesh passes through the "*clean contaminated*" environment of the vagina and therefore is exposed to bacteria and other pathogens during and after implantation.

The amount of mesh used in sacrocolpopexy is significantly less than that typically used in the Prolift System and other transvaginal mesh POP repair procedures. The anatomical location of the mesh and the forces applied to the mesh during implantation also differ between the two procedures. In sacrocolpopexy, the mesh does not need to be inserted through the use of cannulas and is therefore much less likely to experience folding or roping during insertion. Unlike transvaginal procedures, which are done blindly through the use of trocars, sacrocolpopexy allows the surgeon to visualize the placement of the mesh, which avoids the risks of blind passage. For all of these reasons, the risk profile of sacrocolpopexy is superior to that of transvaginal mesh kits for POP, including the Prolift System.

2. Transvaginal Mesh Kits for POP

Use of transvaginal synthetic mesh for POP repair was marketed mainly as a way to increase the durability of the POP repair relative to the misperceived higher failure rate of traditional, non-mesh transvaginal POP surgery. A brief comparison is warranted between the traditional, transvaginal non-mesh POP surgery and the prepackaged mesh kits in order to understand the new and unique treatment alternative the mesh kits represented upon their introduction to the marketplace. The general similarities between traditional, transvaginal and mesh kit POP procedures are:

- Both are designed to treat POP;
- At the time of surgery, the patient is placed in the same position on the operating table;
- The procedures are done under either general or spinal anesthetic;
- The procedures are performed through the vagina; and,
- A cystoscopy is required when performing an anterior or apical repair to rule out inadvertent bladder injury.

Traditional non-mesh transvaginal POP surgery diverges from mesh kit procedures at this point. Typically, traditional surgery, instead of using a synthetic mesh to hold up the prolapsing pelvic organ, uses only sutures (also called stitches) placed into the native tissues surrounding the prolapsing portion of the vagina to repair the POP. These stitches are placed under direct

vision, meaning the surgeon can visualize where the stitch is going, thereby reducing the risk of injury to surrounding tissues and pelvic organs.

In general, there are several broad, though very important differences between traditional, transvaginal non-mesh and mesh kit POP surgeries:

- No synthetic, non-absorbable meshes are used in traditional POP surgery;
- No trocars/guides are used to place the mesh into position in traditional POP surgery;
- There is no tensioning of mesh arms with traditional surgery, and;
- The traditional procedure is performed under direct vision, meaning that the surgeon can see what he/she is doing with no blind passing of trocars.

VI. ETHICON MESH

A. Prolene Mesh

Ethicon first developed sheets of Prolene mesh that could be cut to a desired shape by surgeons, for the surgical treatment of hernias. Shortly thereafter, the same mesh became available for use as the Prolene Hernia System, which is described as a sterile, pre-shaped three-dimensional patch constructed of an undyed Prolene polypropylene mesh constructed of knitted, non-absorbable polypropylene monofilaments identical to those used in Prolene polypropylene nonabsorbable surgical sutures manufactured by Ethicon. Ethicon has reported that this material, when specifically used as a suture (stitch), is nonreactive and retains its strength indefinitely. The Prolene sheets and Prolene Hernia Systems were introduced in the 1990's and were designed and "*... indicated for the repair of hernia or other fascial defects that require the addition of a reinforcing or bridging material to obtain the desired surgical result.*"

As early as 2000, Ethicon employees understood the importance of mesh characteristics, including the importance of pore size and its relation to tissue incorporation. Yet, despite this information, the pore sizes of the Prolene Soft Mesh vary significantly within the mesh. Ultimately, Ethicon stated that the pore sizes (in area) for the Prolene Soft Mesh ranged somewhere between 0.29 mm^2, 0.34 mm^2, 1.08 mm^2, 1.29 mm^2, 1.70 mm^2, and 2.38mm^2 before implantation in the body; but according to Ethicon employees, Ethicon never measured the diameters of the various pores of the Prolene Soft mesh either before or after stretch.[34]

B. Gynemesh Prolene Soft (Gynemesh PS)

In 2000, Ethicon received 510(k) clearance from FDA to market and sell Prolene Soft Mesh, sheets of lighter-weight Prolene that could be cut to a desired shape by surgeons for the surgical treatment of hernias. The stated intended use of Prolene Soft Mesh was for repair of "*abdominal wall hernias or other fascial defects that require additional reinforcing or bridging material for adequate repair*". The mesh is constructed of knitted filaments of polypropylene

[34] Burkley Depo 10/2/2012 and exhibits thereto

identical in composition to those used in Prolene polypropylene, nonabsorbable surgical sutures manufactured by Ethicon. The mesh was reported to have been constructed of reduced diameter monofilament fibers, knitted into a unique design which resulted in a mesh that was approximately 50% more flexible than standard Prolene mesh. The Prolene Soft 510(k) document mirrors the language from Prolene by stating "*this material, when used as a suture, has been reported to be non-reactive and to retain its strength indefinitely in clinical use.*"

Prolene Soft construction was reported as being knitted by a process, which interlinks each fiber junction, which will provide for elasticity in both directions (*bi-directional*).[35,36,37,38,39,40]. This stated "*bi-directional*" elastic property, if accurate, would theoretically allow the mesh to adapt and move so as to accommodate the various stresses encountered in the body. Ethicon documents indicate that this stated bi-directional elastic property would appeal to implanting physicians when choosing the most appropriate treatment option for their patients given the dynamic nature of the female pelvis.

In 2002, Ethicon received 510(k) clearance of Gynemesh Prolene Soft Mesh (Gynemesh PS) which is the exact same mesh as Prolene Soft Mesh. Nonclinical laboratory testing was not performed on the Gynemesh PS product since Ethicon took the position that felt there was no change in the intended clinical use (abdominal wall hernia repair and other fascial defects) when compared to the predicate devices. The mesh is stated to have been designed to provide maximum strength, durability, and surgical adaptability with sufficient porosity for necessary tissue ingrowth.[41] It has been well documented that mesh characteristics and qualities are paramount for successful outcomes.[42,43,44,45,46,47,48,49] With this knowledge, Ethicon inaccurately advertised that Gynemesh PS had "*Large pore size [which] fosters tissue incorporation.*"[50]

Published clinical data on the use of Prolene Mesh and Mersilene mesh was submitted to support the use of these materials as reinforcing or bridging materials in fascial deficiencies of the pelvic wall. Gynemesh PS (identical to Prolene Soft Mesh) was marketed heavily by Ethicon

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[35] ETH.MESH.00015699 - 00015706
[36] ETH.MESH.00013506
[37] Walji Deposition p. 471-472
[38] Robinson Deposition 3-14, p. 683-684
[39] Kirkemo Deposition 4-18, p.246-247
[40] Ciarroca Deposition 3-29, p.264
[41] ETH.MESH.00797 - 00927
[42] Robinson Deposition 3-13, p. 129
[43] Kirkemo Deposition 4-18, p.125-131
[44] de Tayrac R, Gervaise A, Chauveaud A et al: Tension-free polypropylene mesh for vaginal repair of anterior vaginal wall prolapse. J Reprod Med. 2005 Feb;50(2):75-80.
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[46] Milani R, Salvatore S, Soligo M, et al. Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with prolene mesh. BJOG. 2005 Jan;112(1):107-11.
[47] Ganj F, Ibeanu O, Bedestani A et al: Complication of transvaginal monofilament polypropylene mesh in POP repair. Int Urogynecol J Pelvic Floor Dysfunct. 2009 Aug;20(8):919-25. Epub 2009 Apr 7.
[48] Carey M, Higgs P. Vaginal repair with mesh vs colporrhaphy for prolapse a randomized controlled trial. BJOG. 2009 Sep;116(10):1380-6.
[49] Collinet P, Belot F, Debodinance P et al. Transvaginal mesh technique for pelvic organ prolapse repair: mesh exposure management and risk factors. Int Urogynecol J (2006)17:315-320.
[50] ETH-00253

to gynecologists, urologists and urogynecologists as a mesh "*uniquely*" designed and "*Technically advanced by design*" and "*uniquely permanent...*" to meet the needs of POP repair surgery.

In March of 2005, Ethicon launched its first pelvic floor repair kit, Prolift. Ethicon marketed and sold Prolift in the United States for more than three years without obtaining clearance by the FDA. At the demand of FDA, Ethicon subsequently submitted its 510(k) pre-market notification application to FDA seeking permission to sell and market Prolift in the United States.

In May of 2008, more than three years after Ethicon began marketing Prolift, they received 510(k) clearance for both Prolift and Prolift +M. The Prolift kit uses Prolene Soft Mesh (intended for hernia repair) and the Prolift+M kit uses Ultrapro (intended for hernia repair).

C. Prolift Pelvic Floor Repair System

1. General Product Descriptions

The use of transvaginal synthetic mesh for POP repair through the Prolift procedure was marketed by Ethicon primarily as a way to increase the durability of the POP repair relative to the misperceived and grossly exaggerated "higher" anatomic recurrence rates of traditional, non-mesh transvaginal POP surgery. In point of fact, this foundational premise for the marketing of this device was based on several significant items of misinformation. First and foremost, reliance on anatomic recurrence rates as the basis for evaluating the success or failure of a prolapse repair procedure is not valid. The issue is whether or to what extent a recurrence is symptomatic or, in other words, affects the quality of life of the woman. For example, stage 2 prolapse after a prolapse repair is considered to be an anatomic recurrence and technical failure, yet the overwhelming majority of women with such a recurrence following native tissue repair do not feel the need for further treatment, let alone surgery. Thus, the marketing of the Prolift as a means to reduce anatomic recurrence rates completely missed the point. Unfortunately, this marketing strategy was quite successful with surgeons, and ultimately, even AUGS in Committee Opinion 513 acknowledged that functionality and quality of life must be the touchstone.

Second, Ethicon's studies of the mesh material and the prototype procedure in the Gynemesh PS and TVM studies, respectively, demonstrated anatomic recurrence rates as high as or higher than those reported in the studies selectively chosen and miscited by Ethicon in its effort to establish that the recurrence rates with the traditional procedures were unacceptably high. The recurrence rates in the French TVM study exceeded the 20% recurrence rate (at a one-sided 95% confidence interval) pre-determined by Ethicon to be the bright line cut off for success or failure of the procedure. Pursuant to the internal protocols governing the development of the procedure, this was supposed to result in not marketing the procedure; however, Ethicon simply ignored its own protocol and marketed the Prolift. Parenthetically, this is not an isolated failure to adhere to internal protocols put in place to assure that the procedure was safe and effective and that the risks were outweighed by the benefits. Rather, this is part of a disturbing pattern of ignoring such protocols, including the failure to return the project to the concept phase when it was established at least as early as 2003 that erosion and contraction, as well as

recurrences, were resulting from the mesh material (a litany of documents demonstrate that Ethicon was aware of these problems, and knew that the mesh material was not safe and effective and needed to be replaced as soon as possible per internal scientists like Gene Kammerer and Joerg Holste and the inventors of the procedure Dr. Michel Cosson and Prof. Bernard Jacquetin). In fact, many emails and internal documents show that Ethicon was investigating the use of partially absorbable Ultrapro mesh as a means to reduce sexual function issues and other complications, even before the time the Prolift went to market.

Another example is the complete failure to evaluate all potential risks and complications, and the consequences thereof, as part of the pre-launch design control process, which both Dr. Piet Hinoul and Dr. James Hart have confirmed invalidates that FDA mandated process, and thus, should have required that the Prolift not be marketed. Another example is the failure by Dr. Charlotte Owens to conduct a proper pre-launch evaluation of the Prolift, including but not limited to the failure to prepare an original, heavily-researched and objectively-executed clinical evaluation and clinical expert report, which was yet another requirement before marketing that was ignored.[51]

The Prolift was never adequately studied before or after launch. Due to the novel procedure and the unknown risks of this method of placement of the mesh material, the system should have been investigated as an experimental procedure, at most, and not marketed. In fact, internal documents and the deposition of Price St. Hilaire demonstrate that Ethicon worked "behind the scenes" to get ACOG to revise a February 2007 Practice Bulletin that deemed this and similar procedures to be experimental, deleting the reference to experimental due to concerns over insurance and other payor reimbursements for the surgery. This level of documented manipulation of an important medical society is quite disturbing.[52]

The lack of adequate clinical studies is exemplified by the ultimate withdrawal of the Prolift from the market, which Ethicon clearly stated to the FDA was not a reaction to the risks and lack of safety, but rather a "business decision." The internal documents and deposition of Brian Kanerviko prove that the reason the Prolift was withdrawn from the market was because Ethicon faced a choice of conducting the type of robust clinical study that would have shown just how deficient and unsafe the procedure was, or withdraw the Prolift. In fact, this option was apparently first considered on the day Ethicon received the FDA's 522 order requiring the studies be performed. In this context, the FDA rejected the two RCT's presented by Ethicon as insufficient to prove safety and effectiveness. Rather than performing new studies or submitting different studies to satisfy the FDA's 522 Orders, Ethicon withdrew the Prolift from the market. In short, to date, Ethicon has never submitted studies that the FDA deemed sufficient with respect to the Prolift.[53]

Prolift represents a major departure from the traditional, non-mesh transvaginal POP surgeries. Prior to the marketing of the Prolift, Ethicon marketing executive Steve Bell explained in an email he wrote after attending the first demonstration of the procedure to interested physicians, that performance of the Prolift procedure would require a "major mind

[51] Piet Hinoul Depos 4/5-4/6/12, 9/18-9/19/12, 6/26-6/27/13, 1/13/14 & 1/15/14 and exhibits thereto, James Hart Depo 9/17-9/18/13 and exhibits thereto, Charlotte Owens depo 9/12-9/13/12 & 6/19-6/20/13 and exhibits thereto]
[52] Price St. Hilaire depo 7/11-7/12/13and exhibits thereto]
[53] Brian Kanerviko depo 8/22-8/23/13 and exhibits thereto]

shift," based on the differences with the surgeons' training and experience.[54] In contrast to traditional non-mesh surgery, the Prolift Pelvic Floor Repair System represents a newly described, "revolutionary" surgical technique and, according to the patient brochure, was a complete surgical system for the treatment of all aspects of POP. The Prolift Pelvic Floor Repair System comes to the surgeon as a self-contained kit, complete with surgical instruments, uniquely cut synthetic (hernia) meshes, the procedure, and the IFU containing the purported indications, contraindications, warnings, adverse reactions, and information about how to perform the procedure. There are three separate kits, each designed to treat a specific type of POP:

1. Gynecare Prolift Anterior Pelvic Floor Repair System -- for repair of bladder prolapse (cystocele)
2. Gynecare Prolift Posterior Pelvic Floor Repair System -- for repair of rectum prolapse (rectocele)
3. Gynecare Prolift Total Pelvic Floor Repair System -- for repair of cystocele, rectocele, and vaginal vault prolapse

Each kit is similar except for the shape of the mesh and varying number of surgical components used for inserting and retrieving the mesh into and from the patient's vagina and pelvis. (Fig. 1) Each kit also contains a uniquely made, pre-cut designed to repair a specific compartment of the vagina (Fig. 2).

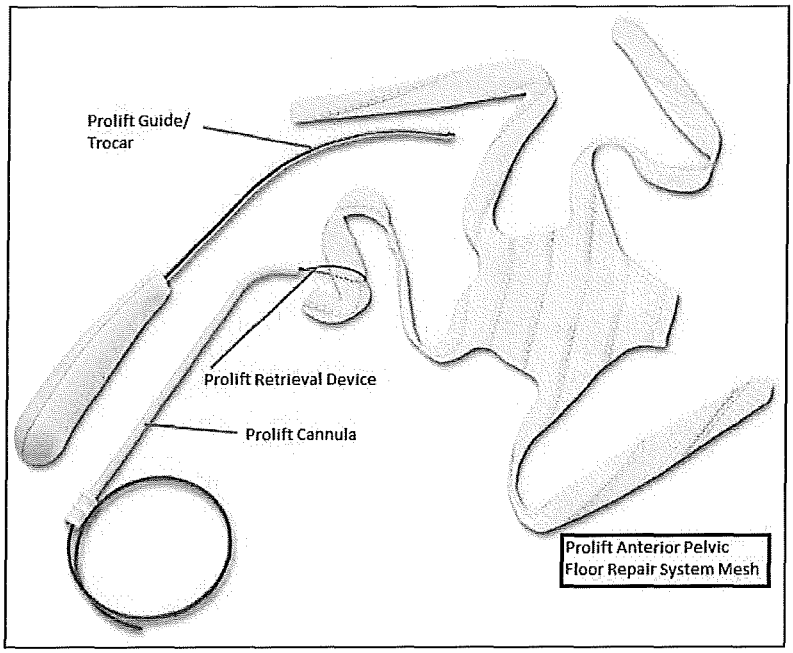

Fig. 1

[54] ETH.MESH.02282833

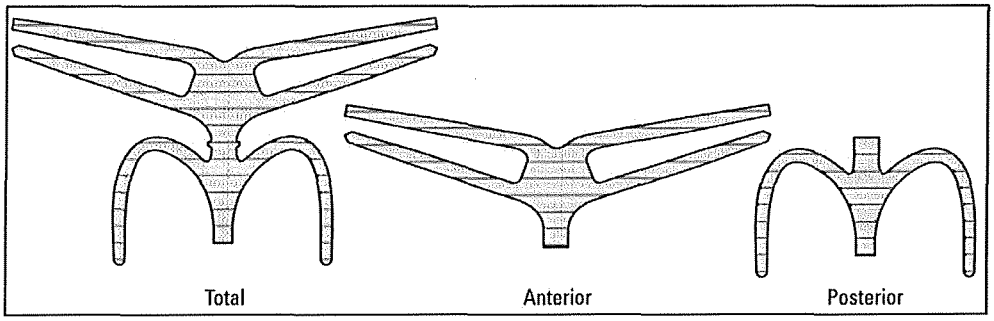

Fig. 2

Each Prolift System kit contains pre-cut mesh composed of non-absorbable knitted filaments of polypropylene identical in composition to those used in Prolene polypropylene, nonabsorbable surgical sutures manufactured by Ethicon. The mesh is reported to have been constructed of reduced diameter monofilament fibers that are knitted into a unique design which resulted in a mesh that is reported to be approximately 50% more flexible than standard Prolene mesh. The Prolift mesh is of identical composition and manufacturing as the Gynemesh PS and Prolene Soft Mesh marketed by Ethicon for us in hernia repair. However, contrary to Prolene Soft Mesh, Prolift meshes were intended to be used for vaginal tissue reinforcement and stabilizations of the fascial structures of the female pelvic floor in vaginal wall prolapse (POP).

Each Prolift System comes with a Performance claim stating that the "*Gynemesh PS elicits a minimum to slight inflammatory reaction, which is transient and is followed by the deposition of a thin fibrous layer of tissue which can grow through the interstices of the mesh, thus incorporating the mesh into adjacent tissue. The mesh remains soft and pliable, and normal wound healing is not noticeably impaired. The material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.*"

2. Prolift Pelvic Floor Repair Systems Components

Along with the synthetic mesh, each kit contains a Prolift Guide/trocar, varying numbers of Prolift Retrieval Devices, and Prolift Cannulas. Each component of the Prolift System is unique and specific to the Prolift Pelvic Floor Repair System.

a) Prolift Guide

The Prolift Guide, also referred to as a "trocar" (Fig. 3) is a single patient, single use surgical instrument specifically designed to create tissue paths to allow the positioning of the meshes of the Prolift Anterior, Prolift Posterior, and Prolift Total. It also is used to facilitate the placement of the Prolift Cannula. Its specific shape, length, design, and curvature were specifically constructed to be used solely with the Prolift and meshes.

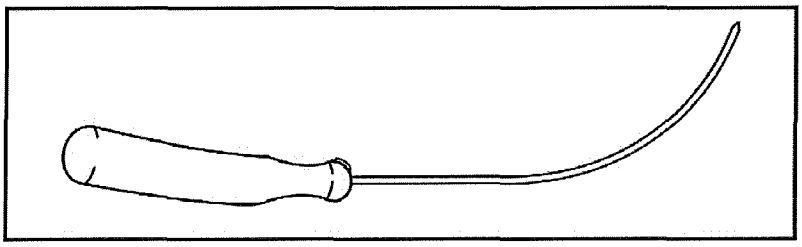

Fig. 3: Prolift Guide

b) Prolift Cannula

The Prolift Cannula (Fig. 4) is a single patient, single use surgical instrument specifically designed to be used in conjunction with the Prolift Guide/trocar to facilitate passage of the Prolift mesh straps in an effort to reduce damage to the surrounding vaginal tissues and pelvic organs. Each Prolift Cannula is placed over the trocar prior to passage and remains in place until after the trocar is removed. The Prolift Cannula's specific shape, length, design, and curvature were specifically constructed to be used solely with the Prolift.

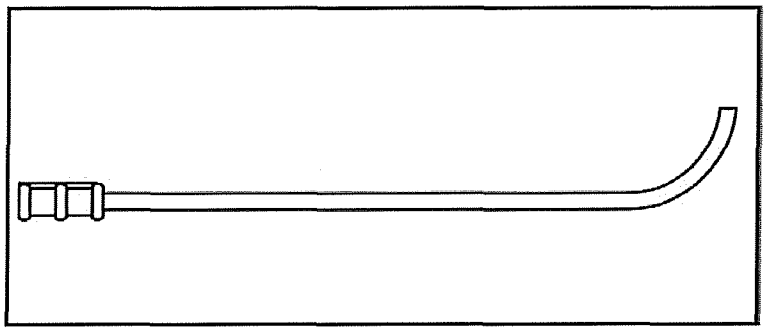

Fig. 4: Prolift Cannula

c) Prolift Retrieval Device

The Prolift Retrieval Device (Fig. 5) is a single patient, single use surgical instrument specifically designed to be used with the Prolift Pelvic Floor System. The Retrieval Device is passed through the previously placed Prolift Cannula until its farthest most end is passed into and through the vaginal dissection area. The farthest most end of the Retrieval Device has a loop to securely fix the mesh implant straps as the strap is withdrawn through the Prolift Cannula. The Retrieval Device's specific shape, length, and design were specifically constructed to be used solely with the Prolift Systems.

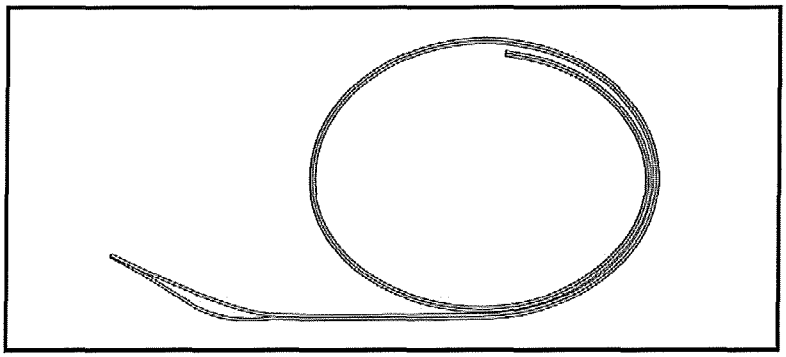

Fig. 5: Prolift Retrieval Device

All the components of the Prolift Pelvic Floor System are packaged so as to be used together, in combination, and not with any other pelvic floor repair kit. The three separate kits (Prolift Anterior, Posterior and Total) and their individual kit variations are briefly outlined below:

d) Prolift Anterior Pelvic Floor Repair System

The Anterior mesh implant (Fig. 2) is constructed of Gynemesh PS and is pre-cut for surgical repair of anterior vaginal wall prolapse (cystocele). The implant has four straps, which are placed and fixed in position via multiple blind Prolift trocar passes through the transobturator route. Each of the pre-cut extension arms of the mesh is designed to permanently reinforce the pubocervical fascia.

The Prolift Anterior Pelvic Floor Repair System kit comes with an included Prolift Guide/trocar (Fig. 2), four Prolift Cannulas (Fig. 3), and four Prolift Retrieval Devices (Fig. 4).

e) Prolift Posterior Pelvic Floor Repair System

The Posterior mesh implant (Fig. 2) is constructed of Gynemesh PS and is pre-cut specifically for repair of the posterior and possibly apical vaginal wall prolapse. The mesh is configured so as to have two straps that are secured into place with blind trocar passages through the sacrospinous ligament via a transgluteal (buttock) approach or modified to be placed via a vaginal approach. Each of the pre-cut extension arms of the mesh is designed to permanently reinforce the rectovaginal fascia.

The Prolift Posterior Pelvic Floor Repair System kit comes with an included Prolift Guide/trocar (Fig. 2), two Prolift Cannulas (Fig. 3), and two Prolift Retrieval Devices (Fig.5).

f) Prolift Total Pelvic Floor Repair System

The Total mesh implant (Fig.2) is constructed of Gynemesh PS and is pre-cut specifically for surgical repair of total vaginal vault prolapse. The implant has six straps; four used for securing the anterior (top) portion of the mesh via blind trocar passage using the transobturator route and two for securing the posterior (bottom) portion of the mesh into the sacrospinous ligament via blind trocar passage using the transgluteal (buttock) route.

The Prolift Total Pelvic Floor Repair System kit comes with an included Prolift Guide/trocar (Fig. 3), six Prolift Cannulas (Fig. 4), and six Prolift Retrieval Devices (Fig. 5).

3. Surgical Technique

One of the unique characteristics of the Prolift Pelvic Floor Repair Systems compared to traditional, non-mesh POP surgeries is that the Prolift Systems are a self-contained surgical "kits" *and* procedures. Prolift Systems is purchased as a complete, packaged entity (kit) complete with a uniquely shaped, pre-cut synthetic, nonabsorbable mesh, varying numbers of Prolift Guides/trocars, Prolift Cannulas, and Prolift Retrieval Devices *and* a Prolift Surgical Guide and IFU.

a) Prolift Anterior Pelvic Floor Repair Procedure

Ethicon maintains that in order to reduce complications, to provide the most appropriate anatomical results, as well as to maintain normal vaginal and pelvic floor function, it is imperative for the mesh arms once surgically inserted to be "*tensioned appropriately*". However, it should be noted that there is no standardized method of measuring "*tension*." By definition, due to the weight of pelvic organs, once the patient is standing, the mesh will no longer be "*tension-free*". Also by definition, the Prolift arms are tensioned from the moment they are implanted and fixed and they begin to compensate for the pelvic forces that the damaged native tissue can no longer compensate for.

b) Prolift Posterior Pelvic Floor Repair Procedure

As with the Anterior Prolift mesh, the appropriate positioning of the mesh, "without tension", is necessary. Ethicon knew that, with this procedure, the surgeon may trim the mesh based upon the specific needs of the patient.

c) Prolift Total Pelvic Floor Repair Procedure

The Prolift Total Pelvic Floor Repair System entails a combination of both the Prolift Anterior and the Prolift Posterior procedures with variations of each making the Prolift Total a unique procedure. Also, the surgeon must make varying perioperative decisions dependent upon whether or not the patient has a uterus and whether or not a hysterectomy is going to be performed at the time of the Prolift Total procedure. The Prolift Total mesh (Figure 2) is supposedly uniquely shaped and specifically designed to address a total vaginal vault prolapse. However, the surgeon must cut the mesh depending on whether the patient has or has not had a previous hysterectomy and whether uterine preserving surgery is to be performed. These are all decisions the experienced surgeon would address preoperatively with the patient. In order to place the Prolift Total Pelvic Floor Repair System, first the Prolift anterior procedure is performed and then, the Prolift posterior procedure is performed. This would leave a total of 6 incisions. As with the Prolift Total Pelvic Floor Repair System, the Prolift Anterior Pelvic Floor Repair System, and the Prolift Posterior Pelvic Floor Repair System, the trocars are passed blindly and can result in serious patient injury. Lastly, the surgeon is then faced with the challenge of attempting to appropriately tension the mesh arms in order to reduce the risk of complications.

4. The Prolift System Constitutes Major Invasive Surgery

The insertion technique for the Prolift System is a complicated one and, even in the hands of the most careful and highly-skilled surgeon, significant complications for the patient can occur. Moreover, there can be little doubt that the implantation of the Prolift System constitutes major invasive surgery and cannot be accurately characterized as "*minimally invasive*" as described in Ethicon's patient brochures.

5. Prolift Surgical Results and Efficacy

POP is a quality of life (QOL) issue. It is rarely, if ever, a life- threatening condition. Therefore, POP surgery "success" needs to be defined as whether or not the POP procedure improves or corrects the symptoms that are bothersome to the patient. A surgeon must counsel the patient and justify the relief of POP symptoms against the pain, recovery time, possibility of complications, and expense of POP surgery. With this baseline understanding, it is imperative to analyze the literally thousands of pages of data that exist describing "success" of surgery. To add confusion to the unsuspecting physician and equally unsuspecting patient, all too often, "success" is reported only in terms of "anatomical" results (whether or not the prolapsed pelvic organ was restored to its native position) and not in terms of "symptomatic" results (whether the patient's POP symptoms were relieved by the POP procedure). Because of this often confusing and misleading reporting style, it is important to review the data focusing on anatomic results versus symptomatic results, and it is important to realize that these two parameters of reported "success" are, by no means, synonymous. Also, it is generally accepted that POP surgical results are essentially meaningless unless they are a minimum of 12 months following surgery, and even 12-month data is of limited value given that the mesh is permanently implanted in a woman's pelvic tissue and considering the fact that many mesh-related complications manifest years after surgery. Any reported results less than 12 months in duration from the time of POP surgery must be considered preliminary, must be reported as preliminary and, by no means, can be suggestive of being permanent Any dogmatic statements correlating or suggesting preliminary results with positive long-term results is purposefully misleading and false.

a) Anatomic Results

Earlier medical literature tended to show that transvaginal anterior mesh POP repair often was able to restore a more normal anatomy compared to traditional non-mesh POP repairs. However, this was only when the strict anatomical stages criteria established by the 2001 National Institutes of Health (NIH) Workshop on Standardization of Terminology for Researchers in Pelvic Floor Disorders were followed. When utilizing the more clinically relevant and contemporary measures of surgical outcomes, the difference in anatomic success becomes negligible. Also of importance is that the risk of complications is higher in the mesh POP repair groups. This fact highlights the critically important issue of the need to balance the anatomic results with mesh-specific complications. Transvaginal mesh posterior and transvaginal mesh apical POP repair procedures do not provide any superior anatomic results compared to traditional, transvaginal non-mesh POP procedures. Also, very interesting data has emerged that shows that women, following POP procedures, that have "perfect vaginal support" actually have a lower QOL and subjective improvement compared with women with lesser degrees of support. This fact points to the dynamic nature of the vagina and indicates the

necessity of maintaining vaginal mobility and elasticity for normal vaginal and pelvic floor functioning.

b) Symptomatic Results

To date, regarding specifically anterior transvaginal mesh POP repairs, there is no conclusive evidence within non-industry supported manuscripts published by reputable, peer-reviewed medical and surgical journals that demonstrates a statistically significant improvement in subjective success, QOL, reoperation rates, and POP symptom relief.

Regarding specifically posterior transvaginal mesh POP repairs, there is also no conclusive evidence within non-industry supported manuscripts published by reputable, peer-reviewed medical and surgical journals, which demonstrates a statistically significant improvement in QOL and POP symptom relief.

Regarding specifically apical transvaginal mesh POP repairs, there is no conclusive evidence within non-industry supported manuscripts published by reputable, peer-reviewed medical and surgical journals, which demonstrates a statistically significant improvement in QOL and POP symptom relief.

6. Summary of Transvaginal Mesh Repair Results

There are insufficiencies in most POP manuscripts (underpowered, insufficient QOL evaluation, industry sponsored, variability of reporting, insufficient follow-up, insufficient duration, endpoints that are related to anatomic results rather than safety concerns, etc.). Previous manuscripts indicated the "anatomic" success of the isolated anterior compartment with mesh and suggested it to be superior to that of traditional non-mesh repairs. However, when utilizing the more clinically relevant and contemporary measures of surgical outcomes, the difference in anatomic success becomes negligible. The success of transvaginal mesh for both apical and posterior POP repair is equivocal compared to traditional non-mesh repairs. Also, what is highly underreported in the data is that even if POP recurrence occurs following surgery, in either the mesh or non-mesh POP repair patients, the POP recurrence is usually low stage, minimally symptomatic, and usually does not require surgical intervention. Ultimately, however, what matters most to the patient, in contrast to anatomic results, is the relief of the POP symptoms that were bothering the woman in the first place. In this very important issue, there is no data demonstrating that transvaginal mesh POP surgery, in any compartment, has been shown to be superior in symptom relief and QOL to that of traditional, non-mesh repairs.

Also, as mentioned above, data demonstrates that women who have "perfect vaginal support" following POP procedures actually have a lower QOL compared with women with lesser degrees of support. This fact points to the dynamic nature of the vagina and indicates the necessity of maintaining vaginal mobility and elasticity in order for normal vaginal and pelvic floor functioning. Therefore, any procedure that impairs or inhibits the vagina or the pelvic floor's normal dynamic, mobile and elastic function can greatly impact the normal function.

As discussed earlier in this report, one of the most common arguments used to justify vaginal mesh use over the traditional, non-mesh POP repairs was the previously reported 30-40% failure rates of the traditional repairs. However, currently, within contemporary POP studies,

which utilize up-to-date prolapse definitions, the accepted failure rate of traditional, non-mesh POP repairs is less than 15% and closer to 12%. Therefore, for the benefit of mesh repairs to outweigh the risks, it would seem imperative for the mesh repairs to provide a clear benefit regarding recurrence rates. In 2006, initial Prolift advertising claimed a "*less than 5% failure rate*" at only three months post-op. However, in Ethicon internal documents it was reported that "*Prof Jacquetin's data has not proved as positive as hoped – showing approx 80% success rate – The data will be initially presented at IUGA in September. Note that this data is a retrospective study of over 100 patients using TVM technique, not necessarily used with Prolift. This less than 90% success rate forces us to differentiate Prolift from the TVM technique moving forward.*" [55] Because of the disappointing results from the French TVM Study by Jacquetin, et al., Ethicon chose not to inform doctors and patients of those longer-term results and, instead, chose to use extremely short-term results. At the same time, Ethicon knew that the French results showed an 18.4% failure rate at 12 months after surgery. Despite knowing these results, Ethicon used only the purported positive information from the TVM study in their marketing, while choosing to withhold negative data.

VII. COMPLICATIONS OF PROLIFT REPAIR SYSTEM – SAFETY

A. Introduction

There is an abundant amount of readily available medical literature with detailed descriptions of the increased number of mesh procedure complications compared to the non-mesh POP procedures. It should be noted that even though the documented complication rate is high with Prolift POP systems, the true incidence is not known due to multiple factors including the critical reality that complications are vastly underreported, with some articles, including one by the former Commissioner of the FDA, estimating that complications are underreported at a rate of 100 to 1. [56] Some mesh-specific complications are devastating to the patient, her sexual partner, and to the overall medical financial burden. Furthermore, some complications are permanent, resulting in lifelong harm and disability to the patient and her partner.

Several factors come into play regarding the increased complication rate with the Prolift POP repair systems. The blind insertion of the trocars into and through deep pelvic structures such as the obturator foramen, ischiorectal fossa, ileococcygeus muscle and the sacrospinous ligament exposes the patient to an increased risk of injury to the rectum, bladder, inferior gluteal blood vessels, pudendal nerve, pudendal artery and vein, and the sciatic nerve. Also, the very presence of large quantities of synthetic, nonabsorbable mesh placed via a transvaginal incision increases the risk of various complications.

Furthermore, the surgeons' role in performing POP surgery is complicated and does play a role. However, even highly-qualified, high-volume, top-tiered Prolift surgeons report high complication rates relative to both traditional, non-mesh POP as well as mesh repairs using Prolift. The fact that Ethicon specifically targeted "second tier" surgeons to whom they would aggressively market the Prolift only added to the complexities of marketing this "revolutionary"

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[55] ETH.MESH.00741137

[56] Kessler, D: Introducing a New Approach to Reporting Medication and Device Adverse Effects and Product Problems: JAMA, June 2, 1993 – Volume 269, No 21

surgical device and technique to a surgeon population that in many cases, had no idea how to treat the complications that would ensue and that were not warned about by Ethicon.

There is some confusion and misleading documentation discussing whether or not a given mesh-related complication is defined as "rare" or not. There is no single, widely accepted definition for "rare". In the United States, however, the *Rare Disease Act* of 2002 defines a rare disease strictly according to its prevalence within the community, specifically "*any disease or condition that affects... about 1 in 1,500 people*." In Japan, the legal definition of a rare disease is one that affects about 1 in 2,500 people. The European Commission on Public Health has defined a rare disease as a condition that occurs in a low prevalence, which they defined as less than 1 in 2,000 people affected. The definitions used in the medical literature and by national health plans are similarly divided, with definitions ranging from 1/1,000 to 1/200,000. Ethicon's own internal documents define "rare" as 1/100,000.[57] *Based upon these criteria, many, if not most of the mesh-related complications do not fit the definition of "rare".*[58,59]

B. Impaired Vaginal Healing

At the onset of transvaginal synthetic mesh use for POP, there was confusion in the literature and at scientific meetings as physicians and patients encountered a new set of previously undescribed, mesh-related vaginal complications. Because of this confusion, many early documents underreported or did not report certain complications at all. This may account for vastly differing complication rate results in the literature and the underreporting of complication rates in many reports. Therefore, as a result of the emergence of mesh-specific complications and for clarification and reporting purposes, medical literature has generally adopted descriptive nomenclature (mesh granulation, mesh extrusion, mesh erosion) pertaining to poor mesh healing in the vagina.

Mesh "*granulation*" or "*wound granulation*," indicates poor vaginal wall healing and possible mesh infection. Symptoms of wound granulation may include foul smelling vaginal discharge, bloody vaginal discharge, pelvic discomfort, pelvic pain, vaginal wound infection and dyspareunia.

It is generally accepted that mesh "erosion," "*extrusion*" and mesh "exposure" indicates that the inflammation created by the synthetic mesh has impaired vaginal tissue to such a degree so as to cause the mesh to actually be exposed through the vaginal wall. Symptoms may include foul smelling vaginal discharge, bloody vaginal discharge, pelvic discomfort, pelvic pain, vaginal wound infection and dyspareunia. In some patients, the synthetic mesh has worn through the wall of the urethra (the tube urine passes through from the bladder), or the wall of the bladder or the rectal or intestinal wall. This complication can be possibly life threatening. Additional symptoms include foul smelling vaginal discharge, bloody vaginal discharge, pelvic discomfort,

[57] ETH.MESH.003088817
[58] Gauld depo 4/26/12 197:23-200:15
[59] Hinoul Deposition 4-5-12, p70-72.

pelvic pain, pain with urination, vaginal wound infection, dyspareunia, bowel function abnormalities, bloody bowel movements, bladder infection, fever, and sepsis.[60]

It is probable that wound granulation, vaginal extrusion, and bladder/urethral erosion represent a spectrum of the same problem, with the only difference being the degree to which the impaired healing between the mesh and vagina/bladder has been allowed to proceed. To place each of the mesh "epithelial" complications into separate categories is misleading and minimizes their total number.[61] That said, wound granulation is a relatively common complication and has been reported in ~2-12% of patients. The management of this problem can be minor with most patients being treated with conservative measures and reassurance. Vaginal mesh extrusion has been reported to occur in 10-33% of patients. If this rate were truly accurate, this would represent an estimated 3,750 to 7,500 women per year in the United States in 2010 alone. Highly skilled, high-volume POP surgeons reported a vaginal extrusion rate of up to 12%. Therefore, the argument that vaginal extrusion is limited or solely due to surgeon inexperience does not hold true when examining the available literature.

Treatment ranges from observation alone in mild cases to estrogen therapy and antibiotics. If conservative measures fail or the size of the mesh extrusion is too great or the patient's symptoms are too significant, then a surgical procedure to remove the exposed vaginal mesh is necessary. It is estimated that 75% of patients that present with vaginal mesh extrusion will ultimately require some form of surgical repair and excision of the exposed mesh.[62] Unfortunately, simple surgical removal is not always successful and creates even further risk of injury to the patient including, but certainly not limited to, vesicovaginal fistulas (a hole between the bladder, rectum and vagina). This problem requires extensive, complicated, and advanced surgery to repair, prolonged recovery for the patient and significant added medical expense.[63,64,65,66]

Ethicon's Device Design Safety Assessment states that the probability of hazard for postoperative tissue erosion is occasional (1 in 10,000 maximum). However, by 2006, there was abundant evidence in the literature describing mesh complications with erosions at a significantly

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[60] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15.

[61] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15.

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[64] Deffieux X, De Tayrac R, Huel C, et al. Vaginal mesh erosion after transvaginal repair of cystocele using Gynemesh or Gynemesh-Soft in 138 women: a comparative study. Int Urogynecol J Pelvic Floor Dysfunct. 2007 Jan;18(1):73-9.

[65] Firoozi F, Goldman H. Transvaginal excision of mesh erosion involving the bladder after mesh placement using a prolapse kit - a novel technique. Urology. 2010 Jan;75(1):203-6.

[66] Abed H, Rahn D, Lowenstein L, et al. Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. Int Urogynecol J. 2011 Jul;22(7):789-98.

higher rate.[67,68,69,70,71,72,73,74] Ethicon internal documents and studies indicate that postoperative vaginal erosion/extrusion/exposure occurred in 13.7% of cases (U.S. TVM arm = 14.1%; and French TVM arm = 10%). Over 50% of these exposures required surgical treatment.[75,76,77,78,79,80]

In the Prolift patient brochure, FDA requested that Ethicon "include a statement under the '*What are the risks?*' section (p.13) which reflects that one of the most common adverse event[s] is mesh extrusion [exposure] and this complication usually requires the removal of the mesh and may interfere with sexual function".[81] Instead of following the FDA's request, Ethicon changed this section to state, "*There is also a risk of the mesh material becoming exposed in the vaginal canal.*" They also ignored the FDA's request when they stated, "*This information is based on our Medical expert's input on the standard means of treating mesh exposures, many of which resolve spontaneously or with medication.*" Of course, the medical literature at the time (May 2008) indicated that virtually no cases of mesh exposure resolve "*spontaneously*." A literature search for mesh exposure through May 2008 demonstrates an overall 221 mesh exposures in 2138 patients (10.3%). Of those patients, 130 of 195 (66.7%) required mesh excision after exposure. [82,83,84,85,86,87,88,89]. Mesh erosions were such a frequent and severe reported

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[67] Bader G, Fauconnier A, Roger N et al: Cystocele repair by vaginal approach with a tension-free transversal polypropylene mesh. Technique and results. Gynecologie Obstetrique & Fertilite 32 (2004) 280-284.
[68] Milani R, Salvatore S, Soligo M, et al. Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with prolene mesh. BJOG. 2005 Jan;112(1):107-11.
[69] De Tayrac R, Gervaise A, Chauveaud A et al: Combined genital prolapse repair reinforced with a polypropylene mesh and tension-free vaginal tape in women with genital prolapse and stress urinary incontinence: a retrospective case-control study with short-term follow-up. Acta Obstet Gynecol Scand. 2004 Oct;83(10):950-4.
[70] De Tayrac R, Gervaise A, Chauveaud A et al: Tension-free polypropylene mesh for vaginal repair of anterior vaginal wall prolapse. J Reprod Med. 2005 Feb;50(2):75-80.
[71] Jacquetin B, Cosson M, Lucente V et al: Prospective clinical assessment of the transvaginal mesh (TVM) technique for treatment of pelvic organ prolapse-one year results of 175 patients. (Abstract #291: Presentation International Continence Society 2006).
[72] Benhaim Y, de Tayrac R, Deffieux X, Gervaise A et al: Treatment of genital prolapse with a polypropylene mesh inserted via the vaginal route. Anatomic and functional outcome in women aged less than 50 years. J Gynecol Obstet Biol Reprod (Paris). 2006 May;35(3):219-26.
[73] Cosson M, Debodinance P, Boukerrou M et al: Mechanical properties of synthetic implants used in the repair of prolapse and urinary incontinence in women: which is the ideal material? Int Urogynecol J (2003) 14:169-178.
[74] Debodinance P, Engrand J. Development of better tolerated prosthetic materials: applications in gynecological surgery. J Gynecol Obstet Biol Reprod (Paris). 2002 Oct;31(6):527-40.
[75] ETH.MESH.00081035
[76] ETH.MESH.00081083
[77] ETH.MESH.00080954
[78] ETH.MESH.00081006
[79] ETH-01121 – 01122
[80] ETH.MESH.00081000 – 00081001
[81] ETH-01322
[82] Milani R, Salvatore S, Soligo M, et al. Functional and anatomical outcome of anterior and posterior vaginal prolapse repair with prolene mesh. BJOG. 2005 Jan;112(1):107-11.
[83] De Tayrac R, Gervaise A, Chauveaud A et al: Tension-free polypropylene mesh for vaginal repair of anterior vaginal wall prolapse. J Reprod Med. 2005 Feb;50(2):75-80.
[84] De Tayrac R, Deffieux X, Gervaise A et al: Long term anatomical and functional assessment of trans vaginal cystocele repair using polypropylene mesh. Int Urogynecol J Pelvic Floor Dysfunct. 2006 Sep;17(5):483-8.
[85] Collinet P, Belot F, Debodinance P et al. Transvaginal mesh technique for pelvic organ prolapse repair: mesh exposure management and risk factors. Int Urogynecol J (2006) 17:315-320.

complication that Ethicon's internal documents are filled with internal studies and emails, presentations, design change considerations, retention of external consultants and meetings at high levels within the company in attempts to address this serious adverse complication in women's pelvic tissues. [90]

C. Continuous Organ Injury

Ethicon's Device Design Safety Assessment (DDSA) also states that the expected risk of vital organ perforation with the Prolift procedure is "*rare*" (1 in 100,000 maximum). However, injury to adjacent pelvic organs is *not* rare and has been reported to occur in as many as 3-6.6% of pelvic mesh patients implanted with the Prolift System. This is due to the fact that the female pelvis is tightly packed with multiple anatomic structures in very close spatial proximity. This spatial arrangement demands the highest surgical skill even without multiple blind passes into the deep pelvic spaces with trocars contained in the Prolift System. Even the surgeons involved in the TVM study (4 years, 600 patients) had 1.9 % bladder and other organ perforations. Ethicon's website listed 1.9% bladder perforations, 1.2% rectal perforations and urethral damage 0.5% for a combined total of 3.6% perforations. Despite these known rates of complications of organ perforation by Ethicon, its DDSA was apparently never updated with accurate figures, and more importantly, this high rate of complications was not properly communicated to surgeons or patients.

All Prolift trocars are passed blindly and, even in highly trained surgical hands, serious injury can result to the bladder, ureter, pelvic nerves, and potentially life-threatening injury to major pelvic blood vessels can occur. This issue takes on even far greater importance when considering the varying level of skill and experience many surgeons have with the Prolift System. Additionally, if blood vessels are damaged, it may be difficult, if not impossible, to recognize and treat such injuries as they are likely to be deep within the woman's pelvis.[91,92,93,94]

D. Bladder Injury/Perforation

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[86] Deffieux X, De Tayrac R, Huel C, et al. Vaginal mesh erosion after transvaginal repair of cystocele using Gynemesh or Gynemesh-Soft in 138 women: a comparative study. Int Urogynecol J Pelvic Floor Dysfunct. 2007 Jan;18(1):73-9.

[87] Fatton R, Amblard P, Debodinance P. Transvaginal repair of genital prolapse: preliminary results of a new tension-free vaginal mesh (Prolift technique)--a case series multicentric study. Int Urogynecol J Pelvic Floor Dysfunct. 2007 Jul;18(7):743-52.

[88] Altman D, Tapio V et al. Short-term outcome after transvaginal mesh repair of POP. Int Urogynecol J (2008) 19:787–793.

[89] Abdel Fattah I, Ramsey I. Retrospective multicentre study of the new minimally invasive mesh repair devices for POP. BJOG. 2008 Jan;115(1):22-30.

90 ETH.MESH,07192929, ETH.MESH.02270724, ETH.MESH.00584846, ETH.MESH.01220730, ETH.MESH.02157879, ETH.MESH.00006636, ETH.MESH.07200382

[91] ETH.MESH.PM.000019

[92] Chen C, Gustilo-Ashby AM et al. Anatomic relationships of the tension free vaginal mesh trocars. Am J Obstet Gynecol. 2007 Dec;197(6):666.e1-6.

[93] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15.

[94] Vierhout M, Withagen M, Futterer J: Rectal obstruction after a vaginal posterior compartment polypropylene mesh fixed to the sacrospinous ligaments. Int Urogynecol J (2011) 22:1035–1037.

Bladder perforation by the Prolift trocars tends to be one of the more common injuries with a reported incidence of up to 6%. Due to the obvious frequency of bladder perforation, Ethicon should have required from the outset that cystoscopy be performed at the time of the Prolift POP surgery in order to detect and treat a bladder perforation should one exist. An unrecognized bladder perforation undoubtedly leads to a significant number of complications that could otherwise be avoided by cystoscopy.[95,96,97,98]

E. Rectal Injury/Perforation

The incidence of rectal perforation at the time of Prolift POP procedures is less common than those of bladder perforation with a known reported incidence of 0.4-1.2%. Although rectal perforation is less common, the potential severe consequences of a rectal perforation, especially one that goes unrecognized, can be devastating and life threatening. Also, rectal obstruction and rectal-vaginal fistula following the implantation of the Prolift System have been reported. These potentially devastating complications require immediate and skilled intervention to prevent severe complications including death. Following both the Prolift Posterior and the Prolift Total POP procedure, a rectal exam should be performed to check for inadvertent rectal cuts or perforations and to ensure that there has not been any narrowing of the rectum.[99,100,101,102]

F. Vascular Injury

Several sets of major blood vessels (the pudendal, the obturator and the inferior gluteal) are at significantly increased risk for intraoperative injury compared to traditional, non-mesh, and non-trocar POP procedures. These large, major blood vessels are at increased risk due to their close anatomic proximity during the several blind Prolift trocar passages through the pelvic tissue. The internal pudendal artery and vein are at increased risk by the trocar of the Prolift Posterior and Prolift Total Pelvic Floor Repair System because these procedures pass the trocars through the sacrospinous ligament. Any blood vessel injury represents a significant and potentially life threatening condition for the patient. Ethicon's documents indicate awareness of this increased risk at least as early as 2005.[103,104,105]

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[95] ETH-01761
[96] Henderson Deposition 10-5, p457
[97] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15.
[98] Firoozi F, Goldman H. Transvaginal excision of mesh erosion involving the bladder after mesh placement using a prolapse kit - a novel technique. Urology. 2010 Jan;75(1):203-6.
[99] ETH.MESH.PM.000019
[100] ETH.MESH.00067362
[101] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15
[102] Vierhout M, Withagen M, Futterer J: Rectal obstruction after a vaginal posterior compartment polypropylene mesh fixed to the sacrospinous ligaments. Int Urogynecol J (2011) 22:1035–1037.
[103] ETH-48769
[104] Gangam N, Kanee A: Retroperitoneal hemorrhage after a vaginal mesh prolapse procedure. Obstet Gynecol. 2007 Aug;110(2 Pt 2):463-4.

G. Nerve Injury

Pelvic nerve injury is a critically important and under-diagnosed condition following Prolift POP repair. The nerves most specifically at risk are the pudendal nerve and the levator ani nerve. These nerves have critical bladder and pelvic floor functions. However, the pelvic anatomy and specifically the neuroanatomy can vary significantly between patients. Any direct nerve injury during the blind Prolift trocar passage or nerve entrapment by one or more of the Prolift mesh arms can greatly impact the patients' bladder function leading to urinary retention, bladder spasms, urinary leakage and pelvic floor pain syndromes including sexual function dysfunction. Multiple factors increase the likelihood of nerve injury including the multiple blind trocar passes; the close proximity of important nerves to these trocars; and, insufficiently trained or novice surgeons. Specifically, these factors play a role in levator ani nerve injury.[106,107,108,109,110111,112, 113, 114, 115]

The pudendal nerve is susceptible to trocar injury, entrapment, or inflammation secondary to mesh contraction. The pudendal nerve has both sensory and motor function; therefore, when damaged or irritated the pudendal nerve affects both the patient's sensation and the function of key motor/muscle groups. The pudendal nerve crosses the sacrospinous ligament in various locations thereby making it especially susceptible to injury during the blind passage of the trocars. Injury to the pudendal nerve can lead to a painful pelvis syndrome called Pudendal Nerve Neuralgia, which results in a debilitating chronic pelvic pain syndrome.

Despite the knowledge that the Prolift System could damage the pudendal nerve, Ethicon elected not to include a statement regarding the risk of Prolift POP surgery causing "pain with

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[105] Ignjatovic I, Stosic D: Retrovesical haematoma after anterior Prolift procedure for cystocele correction. Int Urogynecol J Pelvic Floor Dysfunct. 2007 Dec;18(12):1495-7. Epub 2007 Jun 29.

[106] ETH.MESH.PM.000019

[107] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15.

[108] Takeyama M, Koyama M, Murakami G et al: Nerve preservation in the tension free vaginal mesh procedures for pelvic organ prolapse - a cadaveric study. Int Urogynecol J Pelvic Floor Dysfunct. 2008 Apr;19(4):559-66. Epub 2007 Oct 10.

[109] Altman D, Zhang A, Falconer C: Innervation of the rectovaginal wall in patients with rectocele compared to healthy controls. Neurourology and Urodynamics 25:776-781.

[110] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15.

[111] Winnard KP, Dmitrieva N, Berkley KJ. Cross-organ interactions between reproductive, gastrointestinal, and urinary tracts: modulation by estrous stage and involvement of the hypogastric nerve. *Am J Physiol Regul Integr Comp Physiol* 291: R1592–R1601, 2006.

[112] Ustinova EE, Fraser MO, Pezzone MA. Colonic irritation in the rat sensitizes urinary bladder afferents to mechanical and chemical stimuli: an afferent origin of pelvic organ cross-sensitization. *Am J Physiol Renal Physiol* 290: F1478–F1487, 2006.

[113] Ustinova et al: Sensitization of pelvic nerve afferents and mast cell infiltration in the urinary bladder following chronic colonic irritation is mediated by neuropeptides. *Am J Physiol Renal Physiol* 292: F123–F130, 2007.

[114] Ruddick CN, Chen MC, Mongiu AK, Klumpp DJ. Organ cross talk modulates pelvic pain. Am J Physiol Regul Integr Comp Physiol 2007;293: R1191–8.

[115] Pezzone MA, Liang R, Fraser MO. A model of neural cross-talk and irritation in the pelvis: implications for the overlap of chronic pelvic pain disorders. *Gastroenterology*128: 1953–1964, 2005.

intercourse and pelvic pain".[116] Also, at the Ethicon Expert Meeting regarding Meshes for Pelvic Floor Repair in June 2006, data was clearly presented which detailed mesh-related nerve damage, the risk of nerve damage, and the consequences of the damage.[117]

H. Urinary Tract Dysfunction and Incontinence

Urination difficulties following Prolift POP procedures include prolonged urinary retention (the inability to void), urinary urgency, urge incontinence, urinary frequency, and new onset stress urinary incontinence (leakage with activity). The incidence of these complications has been reported to occur in as many as 1 in 4 (25%) of women following Prolift POP repair.[118,119,120] Ethicon did not identify voiding dysfunction as a risk in the original Prolift IFU.[121,122,123] However, as early as October 2005, Ethicon's documents show severe and prolonged urinary retention in patients after Prolift surgery. Dr. David Robinson, newly hired into the position of Medical Director at Ethicon, discussed the need to add the risk of postoperative urinary retention to the Prolift IFU. Despite several meetings to consider this, the Prolift IFU was not revised to include this important information until October 2009. As a result, neither physicians nor patients were adequately informed about this potential risk.

Urinary urgency, frequency, and urge incontinence can have a significant negative impact on a woman's quality of life, and the conditions can lead to impaired sleep, impaired sexual function, decreased socialization and depression. Even after the revised Prolift IFU was finally made available in October 2009, Ethicon's statement regarding voiding dysfunction was inadequate in that it was vague and read as if the same risk applied to all pelvic floor repair procedures. This, however, is not the case as the severe and prolonged urinary retention after the Prolift procedure is likely related to the extensive dissection around the sacrospinous ligaments on both the right and left sides of the patient. This extensive dissection, along with the attendant scarring, disrupts the pelvic splanchnic nerves, which normally provide parasympathetic nervous input that controls the bladder's detrusor muscle, resulting in normal detrusor contractions and bladder emptying. Accordingly, the implication in Ethicon's revised IFU for Prolift that the risks

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[116] ETH-80318

[117] ETH-80645-80651

[118] Kasturi S, Diaz S, McDermott C et al: De novo stress urinary incontinence after negative prolapse reduction stress testing for total vaginal mesh procedures: incidence and risk factors. Am J Obstet Gynecol. 2011 Nov;205(5):487.e1-4. Epub 2011 Jul 20.

[119] Roy S, Mohandas A, Coyne K et al: Assessment of the psychometric properties of the short-form prolapse/urinary incontinence sexual questionnaire (PISQ-12) following surgical placement of Prolift+M: A transvaginal partially absorbable mesh system for the treatment of pelvic organ prolapse. J Sec Med 2012;9:1190-1199

[120] Aungst MJ, Friedman EB. De novo stress incontinence and pelvic symptoms after transvaginal mesh repair. Am J Obstet Gynecol. 2009 Jul;201(1):73.e1-7

[121] ETH-80249 (email from David Robinson to Giselle Bonett, description of 4 cases of total Prolift: "In folks with normal preop voiding function, who then post Prolift can can't void [due to bladder atony].... Some have resolved spontaneously but have taken as long as a year to do so.... [t]he cases seem to have no common thread or any difficulty with the surgery Itself. But if this starts getting reported, it is going to scare the daylights out of docs ....")

[122] ETH-01762 ("Dissection for pelvic floor repair procedures has the potential to impair normal voiding for a variable length of time.")

[123] ETH-80297: Jan. 26-27, 2006 email chain about revising the Prolift IFU: "Dissection for Prolift and any similar procedure has the potential to impair normal voiding for variable length of time")

of urinary problems with the Prolift are comparable to that of all pelvic floor repair procedures is misleading at best.

I. Mesh Contraction

Polypropylene surgical mesh is known to contract and shrink when placed in the body.[124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140] Vaginal mesh contraction can result in vaginal fibrosis, infection, chronic vaginal pain, chronic pelvic pain, vaginal shortening, vaginal narrowing, vaginal extrusion, adjacent organ erosion, dyspareunia, recurrence and the need for surgical intervention. The reported incidence (which likely underestimates the degree of the problem) ranges from 11 to 20%. However, because of multiple varying factors such as reporting variations, under-reporting, short-term reporting, patient and physician ignorance, and delayed presentation, it is impossible to know the true incidence and severity of vaginal mesh contraction.[141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160] Feiner and Maher

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[124] ETH-80645 – 80651
[125] Robinson Deposition 3-13, p206
[126] Kirkemo Deposition, p153-154
[127] Walji Deposition p465
[128] Hinoul Deposition 4-5, p132-133
[129] Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia (1997) 1:15-21.
[130] Bouikerrou M, Boulanger L, Rubod C et al: Study of the biomechanical properties of synthetic implanted in vivo. European J. Obstet & Gynecol and Repro Bio 134: (2007) 262-267.
[131] Boukerrou M, Rubod C, Dedet B et al: Tissue resistance of free tension procedure: What about healing? Int Urogynecol J (2008) 19:397-400. Published online Sept 2007.
[132] Klinge U, Klosterhalfen B, Muller M et al: Foreign body reaction to meshes used for the repair of abdominal wall hernias. Eur J Surg. 1999 Jul;165(7):665-73.
[133] Klinge U, Klosterhalfen M, Muller A et al: Shrinking of polypropylene mesh in vivo: an experiment study in dogs. European Journal of Surgery Volume 164, Issue 12, pages 965–969, December 1998.
[134] Klosterhalfen B, Klinge W, Schumpelick V: Functional and morphological evaluation of different polypropylene-mesh modifications for abdominal wall repair. Biomaterials. 1998 Dec;19(24):2235-46.
[135] Klosterhalfen B, Klinge W, Hermanns B et al: Pathology of traditional surgical nets for hernia repair after long-term implantation in humans. [ABSTRACT] Chirugr 2000;71:43-51.
[136] Klosterhalfen B, Junge K, Klinge W. The lightweight and large porous mesh concepts for hernia repair. Expert Rev Med Devices. 2005 Jan;2(1):103-17.
[137] Krambeck A, Dora C, Elliott D. Time-dependent variations in inflammation and scar formation of six different pubovaginal sling materials in the rabbit model. Urology. 2006 May;67(5):1105-10.
[138] Krause H, Galloway S, Khoo S et al: Biocompatible properties of surgical mesh using an animal model. Aust N Z J Obstet Gynaecol. 2006 Feb;46(1):42-5.
[139] Hilger W, Walter A, Zobitz M et al: Histological and biomechanical evaluation of implanted graft materials in a rabbit vaginal and abdominal model. Am J Obstet Gynecol 2006; 195:1826-31.
[140] Garcia M, Ruiz V, Godoy A, et al: Differences in polypropylene shrinkage depending on mesh position in an experimental study. American Journal of Surgery Vol 193, Issue 4, April 2007, p538-542.
[141] ETH.MESH.00067360
[142] ETH-80645 – 80651
[143] Aungst MJ, Friedman EB. De novo stress incontinence and pelvic symptoms after transvaginal mesh repair. Am J Obstet Gynecol. 2009 Jul;201(1):73.e1-7.
[144] Caquant F, Collinet P, Deobodianance P, et al. Safety of transvaginal mesh procedure: retrospective study of 684 patients. J Obstet Gynaecol Res. 2008 Aug;34(4):449-56.
[145] Argirovic RB, Gudovic AM et al, Transvaginal repair of genital prolapse with polypropylene mesh using tension-free technique. Eur J Obstet Gynecol Reprod Biol. 2010 Nov;153(1):104-7.

evaluated 17 women with vaginal mesh contraction to demonstrate that the mesh caused the condition. The patients' presenting complaints included severe vaginal pain, dyspareunia, and focal tenderness over contracted portions of mesh on vaginal examination, mesh erosion, vaginal tightness, and vaginal shortening. The patients underwent surgical intervention with mobilization of mesh from underlying tissue, division of fixation arms of the central graft, and excision of contracted mesh. Fifteen of 17 (88%) patients reported a 'substantial reduction in vaginal pain following explantation, while 11 of 17 (64%) reported 'substantial' reduction in dyspareunia. However, despite Feiner's relative success with mesh explanation, the adverse effects of transvaginal mesh contraction caused permanent life-altering sequelae in 22-46% of patients in this study.

More recently, Letouzey et al. reviewed the long-term changes in pelvic mesh volumes over time using three-dimensional translabial ultrasonography and found mean contraction of 30%, 65%, 85% at follow-up durations of 3, 6, and 8 years, respectively. This study demonstrates that the pathological process that causes mesh shrinkage is progressive and there is a linear evolution of the contraction rate with time.

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[146] Clave A, Yahi H, Hammou J, et al. Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 patients. Int Urogynecol J. 2010 Mar;21(3):261-70.
[147] Blandon RE, Gebhart JB et al. Complications from vaginally placed mesh in pelvic reconstructive surgery. Int Urogynecol J Pelvic Floor Dysfunct. 2009 Feb 10.
[148] Collinet P, Belot F, Debodinance P et al. Transvaginal mesh technique for pelvic organ prolapse repair: mesh exposure management and risk factors. Int Urogynecol J (2006) 17:315-320.
[149] Abed H, Rahn D, Lowenstein L, et al. Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. Int Urogynecol J. 2011 Jul;22(7):789-98.
[150] Deffieux X, De Tayrac R, Huel C, et al. Vaginal mesh erosion after transvaginal repair of cystocele using Gynemesh or Gynemesh-Soft in 138 women: a comparative study. Int Urogynecol J Pelvic Floor Dysfunct. 2007 Jan;18(1):73-9.
[151] Feiner B, Maher C. Vaginal mesh contraction: definition, clinical presentation, and management. Obstet Gynecol. 2010 Feb;115(2 Pt 1):325-30.
[152] Foon R, Toozs-Hobson P, Latthe P. Adjuvant materials in anterior vaginal wall prolapse surgery: a systematic review of effectiveness and complications. Int Urogynecol J Pelvic Floor Dysfunct. 2008 Dec;19(12):1697-706.
[153] Krause H, Bennett M, Forwood M. Biomechanical properties of raw meshes used in pelvic floor reconstruction. Int Urogynecol J Pelvic Floor Dysfunct. 2008 Dec;19(12):1677-81
[154] Dietz H, Vancaillie P, Svehla M. Mechanical properties of urogynecologic implant materials. Int Urogynecol J Pelvic Floor Dysfunct. 2003 Oct;14(4):239-43.
[155] Debodinance P, Engrand J. Development of better tolerated prosthetic materials: applications in gynecological surgery. J Gynecol Obstet Biol Reprod (Paris). 2002 Oct;31(6):527-40.
[156] Martan A, Svabik K. et al. Incidence and prevalence of complications after urogynecological and reconstructive pelvic floor surgery. Ceska Gynekol. 2007 Dec;72(6):410-5.
[157] Jia X, Glazener C, Mowatt G, et al. Efficacy and safety of using mesh or grafts in surgery for anterior and/or posterior vaginal wall prolapse: systemic review and meta-analysis. BJOG 2008 Oct;115(11):1350-61.
[158] Falagas M, Velakoulis S, Iavazzo C, et al. Mesh-related infections after pelvic organ prolapse repair surgery. Eur J Obstet Gynecol Reprod Biol. 2007 Oct;134(2):147-56.
[159] Firoozi F, Goldman H. Transvaginal excision of mesh erosion involving the bladder after mesh placement using a prolapse kit - a novel technique. Urology. 2010 Jan;75(1):203-6.
[160] Diwadkar G, Barber M, Feiner B, et al. Complications and reoperation rates after apical vaginal prolapse surgical repair: a systematic review. Obstet Gynecol. 2009 Feb;113(2 Pt 1):367-73.

At the IUGA Conference in 2009, the inventor of the TVM technique used in the Prolift system, Prof Jacquetin, presented data indicating that painful mesh contraction occurred at a rate of 19.6%. [161]

A consistently worrisome statistic is that many of the complications related to mesh contraction such as pelvic pain and dyspareunia are delayed in onset. Given the currently reported complication rates, there are a large number of women around the world who have yet to develop problems but given enough time will. In other words, we may be seeing just the tip of the iceberg.[162] Ethicon's own internal documents indicate a substantial risk of mesh shrinkage of at least 20% at one year with resultant mesh retraction and vaginal pain.[163,164,165,166,167] However, neither the original Prolift IFU nor the Surgical Guide adequately warned of the risk of mesh contraction. Ethicon also knew from a 2005 article by Cobb et al that "*All available meshes, regardless of their composition, experience a 20-50% reduction in their initial size. Factors of the mesh itself and the surrounding tissue inflammatory response contribute to this phenomenon.*" [168,169]

In addition, the Prolift IFU did not report the negative consequences of mesh contraction, which were known by Ethicon, such as "*vaginal anatomic distortion,*" pelvic pain, vaginal pain, "*negative impact on sexual function,*" "*difficult treatment*" and "*stiffness of the vagina that further impacts sexual function in a negative manner.*" Instead of properly warning of these potential problems, the Prolift IFU misleadingly claimed was that "*the mesh remains soft and pliable, and normal wound healing is not noticeably impaired.*"[170] The Prolift patient information brochure misleadingly stated: *"[Prolift] allows for the restoration of sexual function by restoring vaginal anatomy*".[171] Given the known high rates and amounts of shrinkage, such statements were false and misleading.[172] Physicians were thus misled into believing that contraction was a positive process for the patient, rather than a negative, and in some cases devastating process.

J. Foreign Body Reaction

An abundant amount of medical literature and basic science data over the past 40 years indicates the strong and direct relationship between postoperative complications and mesh design.[173,174,175,176,177,178,179,180,181,182,183,184,185] Reducing mesh-related complications demands a

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[161] L. Velemir, B. Fatton, B. Jacquetin: Mesh shrinkage: How to asses, how to prevent, how to manage. IUGA Como, Italy June 16-20, 2009
[162] ETH-80645 - 80651
[163] ETH-02326
[164] Robison Deposition 3-13, p260
[165] Kirkemo Deposition p153-154
[166] Walji Deposition p465
[167] Hinoul Deposition4-5, p132-133
[168] ETH.MESH.01210562
[169] ETH-80645-80651
[170] ETH.MESH.00095913 - 00095918
[171] ETH-00259
[172] ETH-80645 - 80651
[173] ETH-80645 – 80651
[174] Kirkemo Deposition 4-18, p125-131
[175] Robinson Deposition 3-13, p129-130

thorough understanding and knowledge of the chemical, physical and synthetic characteristics of meshes and how they react inside the human body. Based upon vast amounts of general surgery and basic science literature, there is a consensus that synthetic meshes that are lighter weight, larger pore size, monofilament, and that are capable of maintaining their elasticity and structural stability will have better results with fewer complications. Of all the mesh characteristics mesh porosity, mesh pore size and mesh stability under load are the most important. If a mesh product's design does not allow for effective tissue integration and fibrotic bridging occurs, leading to a rigid scar plate, many adverse events can occur such as erosion, nerve entrapment, pain syndromes, dyspareunia, loss of elasticity, mesh contraction, organ dysfunction and the need for reoperation.[186,187,188,189,190,191,192]

White et al. published an article suggesting that inflammatory response may also be explained by the amount of movement of the implant and mechanical stresses that are placed on the mesh. As the movement and mechanical stresses of the pelvic floor differ extensively to that of the abdominal wall, it should have been obvious to Ethicon that the inflammatory response would not only be different, but also more intense in a pelvic floor implant.

In the late 1990's, studies were published by Klinge et al. in which explanted hernia mesh was analyzed from rats, dogs and humans. They discovered that in some patients, a chronic foreign body reaction could still be observed after 15 years. Given that this implant is meant to be placed permanently in a woman's pelvic tissue, to base the safety and efficacy of Prolift on studies that were short-term (6 months or less in duration), while studies were available in the scientific literature showing potential complications up to 15 years, was irresponsible. Generally

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[176] Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia (1997) 1:15-21.
[177] Bouikerrou M, Boulanger L, Rubod C et al: Study of the biomechanical properties of synthetic implanted in vivo. European J. Obstet & Gynecol and Repro Bio 134: (2007) 262-267.
[178] Klinge U, Klosterhalfen B, Muller M et al: Foreign body reaction to meshes used for the repair of abdominal wall hernias. Eur J Surg. 1999 Jul;165(7):665-73.
[179] Klinge U, Klosterhalfen B, Birkenhauer V: Impact of polymer pore size on the interface scar formation in a rat model. J. Surgical Research 103, 208-214 (2002).
[180] Klinge U, Klosterhalfen M, Muller A et al: Shrinking of polypropylene mesh in vivo: an experiment study in dogs. European Journal of Surgery Volume 164, Issue 12, pages 965–969, December 1998.
[181] Klosterhalfen B, Klinge W, Schumpelick V: Functional and morphological evaluation of different polypropylene-mesh modifications for abdominal wall repair. Biomaterials. 1998 Dec;19(24):2235-46
[182] Klosterhalfen B, Klinge W, Hermanns B et al: Pathology of traditional surgical nets for hernia repair after long-term implantation in humans. [ABSTRACT] Chirugr 2000;71:43-51.
[183] Krause H, Galloway S, Khoo S et al: Biocompatible properties of surgical mesh using an animal model. Aust N Z J Obstet Gynaecol. 2006 Feb;46(1):42-5.
[184] Garcia M, Ruiz V, Godoy A, et al: Differences in polypropylene shrinkage depending on mesh position in an experimental study. American Journal of Surgery Vol 193, Issue 4, April 2007, p538-542.
[185] Cappelletti M, Attolini G, Cangioni G, et al. The use of mesh in abdominal wall defects. Minerva Chir. 1997 Oct;52(10):1169-76.
[186] ETH.MESH.00869977 - 00870098
[187] ETH.MESH.02589033 - 02589079
[188] ETH-80645 – 80651
[189] Robinson Deposition 3-13, p 120
[190] Hinoul Deposition 4-5, p165-170
[191] Robinson Deposition 3-13, p129-130
[192] Kirkemo Deposition 4-18, p138

speaking, the women who undergo these POP mesh procedures are between 30 and 60 years of age. To have a chronic foreign body reaction that can continue for an unmeasured amount of time in a woman who will have this mesh implanted for decades is unsafe and can potentially lead to life-long debilitating pain and complications. Studies that analyzed the complications that occur years after implantation, such as those performed by Klinge and his colleagues, should have provided Ethicon with a more comprehensive understanding of the true long-term risks and complications to patients, and at the very least, should have prompted Ethicon to conduct long-term controlled studies prior to any marketing of the Prolift System.[193,194,195,196,197,198]

Despite the vast amount of data regarding mesh-related inflammatory response, the original and the revised IFU for Prolift claim that "*...implantation of Gynecare Gynesmesh PS mesh elicits a minimum to slight inflammatory reaction, which is transient*".[199,200] However, Ethicon, according to an internal Ethicon email from Scott Jones dated 11-12-2008, knew this was not true because "*Polypropylene creates an intense inflammatory response that results in rapid and dense incorporation into the surrounding tissues...*"[201] The internal Ethicon documents and depositions are filled with references to the chronic foreign body reaction and inflammatory response by the body to the mesh.

K. Degradation

As polypropylene has been used in surgery for over 50 years as a suture material, the mesh in the Prolift System was marketed by Ethicon as inert. However, many published studies and internal Ethicon documents prove otherwise.[202,203,204,205,206,207,208,209,210]

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[193] Klinge U, Klosterhalfen B, Muller M et al: Foreign body reaction to meshes used for the repair of abdominal wall hernias. Eur J Surg. 1999 Jul;165(7):665-73.
[194] Klinge U, Klosterhalfen B, Birkenhauer V: Impact of polymer pore size on the interface scar formation in a rat model. J. Surgical Research 103, 208-214 (2002).
[195] Klinge U, Klosterhalfen M, Muller A et al: Shrinking of polypropylene mesh in vivo: an experiment study in dogs. European Journal of Surgery Volume 164, Issue 12, pages 965–969, December 1998.
[196] Klosterhalfen B, Klinge W, Schumpelick V: Functional and morphological evaluation of different polypropylene-mesh modifications for abdominal wall repair. Biomaterials. 1998 Dec;19(24):2235-46.
[197] Klosterhalfen B, Klinge W, Hermanns B et al: Pathology of traditional surgical nets for hernia repair after long-term implantation in humans. [ABSTRACT] Chirugr 2000;71:43-51.
[198] Klosterhalfen B, Junge K, Klinge W. The lightweight and large porous mesh concepts for hernia repair. Expert Rev Med Devices. 2005 Jan;2(1):103-17.
[199] ETH-00005 (Original)
[200] ETH-01764 (Revised)
[201] ETH.MESH.00087294
[202] ETH.MESH.02589066-02589068
[203] ETH-80645-80651
[204] Robinson Deposition 3-14, p 532-533
[205] Kirkemo Deposition 4-18, p137-138
[206] Klinge U, Klosterhalfen B, Muller M et al: Foreign body reaction to meshes used for the repair of abdominal wall hernias. Eur J Surg. 1999 Jul;165(7):665-73.
[207] Klinge U, Klosterhalfen B, Birkenhauer V: Impact of polymer pore size on the interface scar formation in a rat model. J. Surgical Research 103, 208-214 (2002).
[208] Klinge U, Klosterhalfen M, Muller A et al: Shrinking of polypropylene mesh in vivo: an experiment study in dogs. European Journal of Surgery Volume 164, Issue 12, pages 965–969, December 1998.
[209] Klosterhalfen B, Klinge W, Schumpelick V: Functional and morphological evaluation of different polypropylene-mesh modifications for abdominal wall repair. Biomaterials. 1998 Dec;19(24):2235-46.

Costello et al., in 2007, reported that polypropylene is more susceptible to degradation due to oxidation caused by inflammatory response. Using Scanning Electron Microscopy (SEM), degradation could be seen in PP in the form of cracks and peeling.

Dr. Donald Ostergard, a urogynecologist and founder of AUGS, created a presentation titled "*Polypropylene is Not Inert in the Human Body*" in which he described degradation of in vivo polypropylene.

"Degradation occurs by oxidation";

"A large surface area incites more inflammation";

"This results in more oxidation since more macrophages are present";

Macrophages secrete hydrogen peroxide and hypochlorous acid to oxidize the mesh";

"Mesh may become brittle."

In a 2010 article by Clave et al., 100 pelvic floor explants were analyzed. Results showed an over 20% rate of degradation from the implants. They concluded that "*for transvaginal surgery, clinical experience indicates the use of low density, large pore implants knitted from a monofilament to facilitate tissue integration, and decrease the inflammatory response....not all types of PP implants degraded equally.*" It should be noted that the lead author, Henri Clave, holds an educational position for Ethicon Europe.

In a 2013 article by Wood et al, it was determine that polypropylene material will degrade in vivo due to its exposure to foreign body responses.[211]

As polypropylene degrades, the inflammatory response increases and intensifies.[212,213,214] The abraded fiber surface increases the surface area of the mesh, provides multiple areas that can effectively harbor bacteria, and creates a "*barbed-wire*" effect, all of which lead to an increased risk of an enhanced and chronic inflammatory response, as well as chronic infections due to bacterial proliferation at the mesh surface.

The literature and internal Ethicon studies demonstrate clearly that Ethicon's surgical polypropylene meshes oxidize, degrade, crack and peel in human tissue.[215]

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[210] Klosterhalfen B, Klinge W, Hermanns B et al: Pathology of traditional surgical nets for hernia repair after long-term implantation in humans. [ABSTRACT] Chirugr 2000;71:43-51.

[211] Wood, A. et al. Materials characterization and histological analysis of explanted polypropylene, PTFE, and PET hernia meshes from an individual patient. J Mater Sci Mater Med 24, 1113-22 (2013).

[212] Mamy L, Letouzey V, Lavigne J et al: Correlation between shrinkage and infection of implanted synthetic meshes using an animal model of mesh infection. Int Urogynecol J. 2011 Jan;22(1):47-52.

[213] Boulanger L, Moukerrou M et al. Bacteriological analysis of meshes removed for complications after surgical management of urinary incontinence or pelvic organ prolapse. Int Urogynecol J (2008) 19:827-831

[214] Bellon J, Honduvilla N, Jurado F et al: In vitro interaction of bacteria with polypropylene/ePTFE prostheses. Biomaterials. 2001 Jul;22(14):2021-4.

[215] Liebert T, Chartoff R, Costgrove S. Subcutaneous Implants of Polypropylene Filaments. J.Biomed. Mater. Res. 1976; 10:939-951, Williams D. Review Biodegradation of surgical polymers. Journal of Materials Science. 1982;

Dr. Iakovlev has published numerous articles showing and explaining the degradation and surface cracking of polypropylene explants using histological and transmission electron microscopy approaches.[216]

Not only is this information widely known and accepted in the medical and scientific communities, but it was also known to Ethicon before and at the time of launch of the Prolift System. There are Ethicon studies dating back as far as 1983 using test methods nearly identical to Dr. Iakovlev's showing in vivo degradation of the Prolene polypropylene material.[217] Ethicon conducted additional studies in 1985 (dog study) and in 1987 (human explants); both showing in vivo degradation and cracking of the polypropylene materials.[218]

It is my opinion, to a reasonable degree of medical and scientific certainty that not only does polypropylene degrade in the human body, but failure to warn doctors and patients that Prolift mesh would degrade in human tissue was inexcusable and dangerous to patients and further demonstrates a pattern of Ethicon's refusal to truthfully and accurately communicate known risks and complications of permanent implantation of its Prolift mesh in patients.

L. Pain Syndromes

Persistent pelvic pain (lasting more than 12 weeks after surgery) such as vaginal pain, groin pain, pain with walking, pain with sitting, and pain with sexual activity has been reported as high as 20% of women following Prolift POP repair. Mesh-induced pelvic and vaginal inflammation can lead to nerve irritation due to the mechanical irritation of the mesh and surrounding tissues on the pelvic nerves. This process leads to chronic pain syndromes involving the pelvis, vagina, and buttocks.

The etiology of pain syndromes after Prolift surgery is multi-factorial, given the anatomy and physiology of the pelvic areas affected by the Prolift procedure and the consequences of permanent mesh placement. Chronic pelvic and buttock pain can occur following the implantation of the Prolift system. This is due to a number of reasons including the blind trocar passes through multiple large pelvic muscles, chronic inflammation, contraction of the mesh, nerve entrapment and disruption due to excessive scarring and scar plate formation, nerve trauma and dissection due to surgical implantation of a mesh with sharp edges that curls, ropes, deforms and forms painful ridges in the vagina and surrounding organs. Any or all of the pelvic muscles can be permanently injured or inflamed secondary to the act of the trocars passing through them

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17:1233-1246, Celine Mary, Yves Marois, Martin W. King, Gaetan Laroche, Yvan Douville, Louisette Martin, Robert Guidoin, Comparison of the In Vivo Behaviour of Polyvinylidene Fluoride and Polypropylene Sutures Used in Vascular Surgery, ASAIO Journal, 44 (1998) 199-206, Wood, et al. Materials Characterization and histological analysis of explanted polypropylene, PTFE, and PET hernia meshes from an individual patient. J Mater Sci: Mater med (2013) 24:1113-1122, DEPO.ETH.MESH.00000367, ETH.MESH.09557798, ETH.MESH.15144988, ETH.MESH.00874032, ETH.MESH.07192929, B. Klosterhalfen presentation "What can we learn from explanted meshes?", Depositions of Thomas Barbolt and Daniel Burkley and exhibits thereto

[216] Iakovlev V, Guelcher S, Bendavid R. In Vivo Degradation of Surgical Polypropylene Meshes: A Finding Overlooked for Decades. Virchows Archiv 2014, 463(1): 35; Iakovlev V, Guelcher S, Bendavid R. In Vivo Degradation of Surgical Polypropylene Meshes: A Finding Overlooked for Decades. Virchows Archiv 2014, 463(1): 35

[217] ETH.MESH.15955438

[218] DEPO.ETH.MESH.00004755; ETH.MESH.11336474; ETH.MESH.13334286

and/or secondary to the inflammation caused by the mesh contraction. As a result of this muscular pain, it is not unusual for the woman to be greatly limited in her activities and have a significant negative impact on her QOL. For most of the chronic pain syndromes there is no consistently successful treatment.[219,220,221]

On December 1, 2005, in the notes from the Prolift Round Table Discussion, buttock pain was identified as a complication,[222] but Ethicon did not list postoperative buttock pain as a risk in the original or revised Prolift IFU. In February 2006, Dr. Michel Cosson (a French surgeon who was part of the team that developed the TVM procedure used with the Prolift system) advised Ethicon that a statement should be added to the Prolift IFU about the complication of postoperative pain. However, the Prolift IFU was not revised at that time. The term "pain" was later added to the list of potential adverse reactions, in October 2009. Therefore, Ethicon intentionally withheld information about postoperative pain as an adverse reaction after the Prolift procedure for 3 ½ years. [223] Furthermore, merely listing the word "pain" woefully underdescribes the complex and chronic pain syndromes.

M. Sexual Dysfunction

Painful sexual activity (dyspareunia) and any functional sexual disorder which makes satisfactory sexual activity for the female and her partner painful will have a significant negative impact upon a patient's QOL. Unfortunately, this condition, as well as any other sexual QOL issues, are frequently not studied, are underreported when studied, or completely ignored in the medical literature. The true impact and negative effect on QOL from embarrassment, loss of intimacy, pain, and depression for a woman affected with this condition cannot be truly estimated; but a vast amount of medical literature exists documenting how impaired sexual function significantly impacts a woman's QOL. Therefore, new-onset, post-mesh POP surgery dyspareunia (de novo) rates are underreported, but the reported rates range up to nearly 20%. [224]

The source of dyspareunia and vaginal pain following Prolift POP surgery is multifactorial. The modalities described above can cause general pain and sexual dysfunction. Additionally, the chronic and progressive nature of mesh contraction causing vaginal shrinkage, shortening and fibrosis (firmness) plays a significant role. This condition continues indefinitely such that many patients currently unaffected become affected with time. Depending on the severity of vaginal shrinkage and shortening, outcomes can range from mild sexual discomfort to complete loss of sexual function and inability to accommodate for intercourse.

Also, many studies report only short-term results of less than one year. It is understood that mesh contraction can take many years to develop and this progressive nature of mesh contraction can lead to a delayed onset of dyspareunia and vaginal/pelvic pain. Therefore, there

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[219] ETH-80647 (Lucente prefers "20 recurrences or erosions over 1 pain patient"}
[220] ETH.MESH.00067363
[221] Withagen M Vierhout M, Hendricks J et al: Risk factors for exposure, pain, and dyspareunia after tension-free vaginal mesh procedures. Obstet Gynecol. 2011 Sep;118(3):629-36.
[222] ETH-80636-80644
[223] Walji Deposition 3-4, p 294
[224] Walid MS, Heaton RL: Laparoscopic apical mesh excision for deep dyspareunia caused by mesh banding in the vaginal apex. Arch Gynecol Obstet. 2009 Sep;280(3):347-50.

are more patients who have been treated with Prolift mesh who have not yet developed dyspareunia, but given enough time, will.[225,226,227,228,229] There is no effective treatment for dyspareunia. Despite all available treatment modalities, it is not uncommon for up to 50% of patients to have permanent pain with sexual activity.

Internal emails and meetings at Ethicon both prior to and after the launch of Prolift demonstrate a failure to address this serious condition either through proper warnings to doctors and patients or in design changes to decrease the risk.[230] Despite its knowledge of this very serious complication, Ethicon elected not to warn of the increased risks to sexually active women, or include the statement regarding the risk of Prolift POP surgery causing "pain with intercourse and pelvic pain."[231] As a result of this decision, countless women were, and will be, permanently and needlessly forced to suffer lifelong pain and embarrassment by Ethicon's failure to properly warn of this condition.

N. Frequency of Complications

There is some confusion and often misleading documentation discussing whether or not a given mesh-related complication is defined as "rare" or not. As mentioned earlier in this report, it is important to note that there is no single, widely-accepted definition for "rare." The definitions used in the medical literature and by national health plans are similarly divided, with definitions ranging from 1/1,000 to 1/200,000. Based upon these criteria most of the mesh-related complications do not remotely fit the definition of "rare."[232,233,234] Ethicon defines "rare" as 1/100,000. Ethicon claims that complications due to its mesh products are "rare". But the percentages of serious complications listed in this report are anything but "rare" and many instances occur greater than 10% (1/10) of the time and in other instances 20% (1/5) or more of the time.

In an article published in 2011, a group of physicians were attempting to create terminology and classifications for complications directly related to the implantation of devices into the pelvic floor. The majority of these physicians stated that they were in some way affiliated with medical device manufacturers. Approximately 84 categories were created, showing the large amount of complications that are directly related to mesh products.[235]

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[225] ETH-80645 – 80651
[226] Walji Deposition 3-8, p398-399
[227] Walji Deposition 3-8, p365-366
[228] Gauld Deposition Rough 4-26, p200
[229] Hinoul Deposition 4-5, p200
[230] ETH.MESH.02017152 2007 Expert Meeting; ETH.MESH.00870466: 2006 Expert meeting; ETH.MESH.01220871 email from Kammerer re: D'Art Conversation with Prof. Jacquetin; ETH.MESH.05448541: Email from Susanne Landgrebe re shrinkage review; ETH-18761: email from Kelly Brown re: Proposal for work with CBAT; ETH.MESH.00130117: Email from Ophelie Berthier re ICS Prolift Abstracts
[231] ETH-80318
[232] Gauld Deposition rough 4-26, p 171, p251
[233] Walji Deposition 3-8, p 477
[234] Hinoul Deposition 4-5, p71
[235] Haylen B, Freeman R, Swift S et al: An International Urogynecological Association (IUGA) / International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) & grafts in female pelvic floor surgery. Int Urogynecol J (2011) 22:3–15.

The Prolift surgical kit and procedures are relatively new and unique surgical tools and surgical procedures for POP. Therefore, there is a learning curve associated with their proper performance. In order to reduce complications, to provide the most appropriate anatomical results, and to maintain normal vaginal and pelvic floor function, it is impracticable if not impossible for treating surgeons to have an advanced knowledge of the range of reported complications if "kept in the dark" by manufacturers of these products.

It does not require vast amounts of medical knowledge and experience nor does it require biostatistical analysis to view complications consistently ranging in the 10-20% range as not "rare." Using common sense and the generally accepted definitions of the medical term "rare," most, if not all of the mesh-related complications are "frequent" or "common", but certainly not "rare." Statements suggesting otherwise are misleading to unsuspecting surgeons and patients.[236,237,238,239]

A consistent pattern of significantly increased complication rates of transvaginal Prolift mesh over traditional no-mesh POP repairs is found throughout the medical literature. These complications also come without demonstrable symptomatic or QOL improvement compared to traditional non-mesh surgery. The complications are not "rare" as stated and otherwise implied in the Ethicon IFU documents regarding Prolift. Some complications require repeat surgical intervention to repair the tissue damaged by the effects of the Prolift mesh. Complications such as pelvic pain, buttock pain, vaginal pain, dyspareunia, and pain with walking and sitting have no known consistently successful treatment.

Unfortunately, due to multiple factors, it is very difficult to know the true incidence and severity of many of the mesh-specific complications, but it is clear that they are often underreported. Ethicon withheld information about the frequency of complications in its planned response to the FDA notification.[240] Instead of making efforts to disseminate the very important safety information contained in the FDA notification, Ethicon deliberately downplayed the notification, and instructed its sales staff to refrain from bringing up the FDA notification with physicians.[241] Such instructions are contrary to Ethicon's duty to provide fair and balanced information to physicians and patients regarding the Prolift System.

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[236] Walji Deposition 3-8, p477
[237] Gauld Deposition rough 4-26, p251
[238] Gauld Deposition rough 4-27, p171
[239] Hinoul Deposition 4-5, p71
[240] ETH-47351 (10-15-2008 email about response to FDA notification "...We would prefer not to give reported complication rate for TVT but instead emphasize our commitment to reporting complications")
[241] ETH-47369 (10-21-08 email from Scott Jones about FDA notification to Field Sales Team ".... Also, please note that you are not to proactively initiate conversations with your customers about this notice. If you are asked about the notice, you should respond with the following statement: The complications stated in the notification are known risks that can occur with surgical procedures of this type and they are included in the labeling for our products. If you have further questions, please contact our Medical Affairs group.")

VIII. Product Development

A. Standardized Product & Technique

The attempt at developing a standardized surgical technique for pelvic mesh implantation began with the TVM studies in both the US and France. Ethicon's reasons for proceeding with the launch of Prolift were "supported" by very limited results that were seen during these studies.[242,243,244,245] At the time of launch, only short-term (6-month) results were available. They saw complication rates that were higher than expected; however, Ethicon continued to list them as "rare." Also, as pelvic floor meshes are implanted as a permanent device, it is inappropriate to consider 6-month results a sufficient representation of efficacy and safety, as complications continue to increase with time, as reported by Miller et al. in 2011.[246] The technique used differed between the initial U.S. and French TVM studies. Although, this technique was not considered to be the "final" procedural guide or device, it was their justification for launching Prolift in 2005. In fact, all Ethicon-sponsored articles reporting TVM findings appear to be flawed and misleading.

Ethicon did not submit a 510k premarket notification application to the FDA before marketing Prolift in March 2005. Ethicon was not permitted to market Prolift Pelvic Floor System until FDA clearance in May 2008.[247] It was sold to surgeons and patients for 3 ½ years without proper FDA clearance. No reasonable surgeon would have used the Prolift System had Ethicon disclosed that they had failed to seek or receive proper FDA clearance for this "revolutionary" surgical technique using a "specially designed" pelvic floor mesh. The fact that Ethicon employees acknowledge in internal communications, as cited herein, that the TVM procedure and surgical technique was a "major mind shift" for pelvic surgeons, makes Ethicon's decision not to seek 510k clearance that much more egregious.

B. The IFUs for Prolift Contain the Same Indications as for Gynemesh PS.

The Prolift Systems represented something much different from traditional POP surgery repair as they were developed as a kit (with components like Guides/trocars, Cannulas, Retrieval Devices, and pre-cut mesh implants) and as a new procedure with detailed steps.[248,249,250] As such, multiple new issues of safety and effectiveness were introduced with the Prolift System over and above Gynemesh PS, which was sold simply as a sheet of mesh to be used by the physician as the physician deemed was appropriate.

C. Ethicon Designed Prolift, Not Merely as a Surgical Mesh, but as both a Product *and* a Technique.

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[242] ETH.MESH.02589071
[243] Walji deposition 3-8, p457
[244] Gauld Deposition rough 4-26, p200
[245] Hinoul Deposition 4-5, p200
[246] Walji Deposition p404
[247] ETH-01363 - 01365
[248] ETH-00253 (Gynemesh PS)
[249] ETH.MESH.00095913 – 00095918 (Prolift)
[250] Cosson M, Caquant F et al. Prolift for Pelvic organ prolapse surgical treatment using the TVM group technique - a retrospective study of 687 patients. (ABSTRACT)

Ethicon obtained United States patents for:

- The process of creating a surgical mesh of PP monofilament yarn; [251]
- The shape of the mesh implants and the procedures for placing the mesh implants;[252]
- The system and method for mesh placement (guide, cannula, retrieval, steps of the surgery);[253] and,
- The packaging (precut mesh, etc.). [254]

All of these patents are further evidence of the unique nature of the Prolift product and surgical technique. Ethicon also consistently refers to the "*Prolift procedure*" in its materials, including the IFU and the Prolift surgical technique guide. [255,256,257]

D. Faulty Prolift Product Design and Resultant Complications

There is a scientific correlation between the biophysical characteristics of Prolift mesh and the documented mesh-specific complications of vaginal erosion, extrusion, inflammation, and infection with resultant chronic pain in the pelvis and vagina. [258,259] As a classification for pelvic floor meshes has not been created, the classifications for hernia meshes have often been used. Amid wrote an article in 1997, determining that hernia meshes should have a pore size greater than 75 microns in order to allow for macrophages to clear bacteria; however, his classification did not address scar plating and contraction, and was outdated shortly after publication because "macroporous" or "large pore meshes" did not exist prior to the development of Vypro (Ethicon) mesh, first marketed in 1998. An article was recently published by Klinge et al., which requires a textile porosity greater than 60% in order to be considered 'large pore,' and therefore, allowing for an appropriate level of tissue integration. It is also noted in that publication as well as other scientific literature and numerous Ethicon documents (including Ethicon Medical Affairs Director, David Robinson's draft Clinical Expert Report for Prolift +M) that the pore size of mesh implants needs to be greater than 1mm in all directions in order to allow for proper tissue integration. Inadequate tissue integration caused by inadequate porosity and pore size can reasonably be expected to result in the development of a rigid scar plate, potentially leading to erosion, nerve entrapment, pain syndromes, dyspareunia, and loss of elasticity and mesh contraction. As early as 1998, Ethicon knew and stated repeatedly throughout internal documents that pore size less than 1 mm would result in fibrotic bridging and increased safety risks to patients.

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[251] ETH-07427 - 07433
[252] ETH-07434 – 07494
[253] ETH-07546 - 07609
[254] ETH-07495 - 07545
[255] ETH-00002
[256] ETH-01761
[257] ETH.MESH.00419572
[258] ETH.MESH.02589066-02589068
[259] Kirkemo Deposition 4-18, p135-138

Both during mesh implantation and after, the arms are put under a considerable amount of strain, which may ultimately lead to mesh curling, roping, and/or pore deformation. This creates an even further enhanced state of inflammatory response in the pelvic area.[260,261]

Once a pelvic floor mesh is implanted, the surgeon is unable to see the mesh to know whether it has stayed in a flat position. Wrinkling or curling of the mesh will also prevent adequate tissue in-growth and lead to fibrotic bridging, and increased contraction, and thus, the cascade of chronic inflammatory events, further increasing the risk of complications.

As my practice has evolved to spending almost half my clinical time treating mesh-related complications related to both incontinence slings and POP mesh, I can say that mesh curling, roping, fraying and deforming is a real problem with these meshes. The Prolift mesh, especially the arms, curls and ropes and increases the risk of the cascade of symptoms as set forth throughout this report, with erosion/extrusion, chronic pelvic pain, dyspareunia, organ dysfunction and the need for painful multiple revision surgeries being at the top of the list.

E. Insufficient Prolift Preoperative Guides

Ethicon is responsible for ensuring the safety and effectiveness of products for its intended use and function. Ethicon was marketing not only a new product but also a new surgical procedure.

Ethicon claimed in marketing materials that Prolift was appropriate for almost all patients,[262,263] but it had no clinical evidence to support these claims.

Ethicon claimed that Prolift was appropriate for patients with recurrent prolapse,[264,265] but it was forced to admit that it had no clinical evidence to support this claim during FDA review. Therefore, Ethicon agreed to remove this claim from its labeling.[266] Despite this "agreement," Ethicon continued to make this claim in online Prolift DTC advertising.

Ethicon claimed that a sling procedure to treat SUI could be performed at the same time as the Prolift procedure.[267] However, Ethicon had no clinical evidence to support this claim. In fact, Ethicon had received feedback from experienced Prolift surgeons that the effectiveness of sling procedures was dramatically decreased when performed at the same time as the Prolift procedure.[268] Despite this, Ethicon apparently never studied this issue and never provided this information to surgeons or patients (i.e., that the effectiveness of slings may be decreased with concomitant Prolift procedure).

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[260] Kirkemo Deposition 4-18, p135-138, p150
[261] Hinoul Deposition 4-5, p506-507
[262] ETH-00260
[263] ETH-00264
[264] ETH-00260
[265] ETH-00264
[266] ETH-01321
[267] ETH-00258
[268] ETH-80289 (Email from Steele to Bonet dated 5-10-2006: "decreased efficiency in TVT procedures when treating concomitantly with Prolift. [Dr.] LaSala has had >50% failure rate…")

Ethicon claimed that pain is a symptom of POP,[269,270,271] but they had received feedback from experienced clinicians that pain is not a typical symptom of POP.[272,273] Their marketing materials implied that patients with preoperative pain due to prolapse experienced resolution of the pain after Prolift. However, they had received feedback from experienced Prolift surgeons that patients with preoperative pain often experienced dramatic exacerbation of pain *after* the Prolift procedure.[274,275] Despite this feedback, Ethicon apparently never specifically studied this issue. Ethicon never provided guidance to surgeons or patients regarding the appropriate evaluation and management of patients with pain and prolapse.

Ethicon also marketed to overweight and elderly patients, claiming the procedure was appropriate for them;[276,277,278] but, this claim was never studied and thus, Ethicon had no clinical evidence to support claims that Prolift was a reasonable and appropriate procedure for overweight or elderly patients.

Ethicon stated in the IFU for the TVT (Tension-Free Vaginal tape for urinary incontinence) product line that these products should not be used on patients who are on anti-coagulation therapy (blood thinners such as aspirin, Coumadin, Plavix®). This is because of the blind trocar passages (one on each side) and the inherent bleeding risk this presents. However, the Prolift procedure involves up to six (6) blind trocar passes, and despite anti-coagulation patients' increased risk of bleeding with these trocar passes, Ethicon chose not to warn against this risk in its original Prolift IFU.[279] Although working drafts of the original IFU contained the statement, "*Do not use the Gynecare Prolift Pelvic Floor Repair Systems in patients who are on anti-coagulation therapy*,"[280] this statement was subsequently deleted.[281,282] Ethicon eventually revised the IFU to say that patients on anticoagulation should be "*carefully managed*."[283]

F. Inadequate Prolift Pelvic Floor System Surgical Training

A marked difference exists between the Prolift Pelvic Floor System (both product and procedure) and the traditional non-mesh POP repair surgery. This fact was emphasized in Ethicon's product evaluations *before* Prolift was commercially available and in feedback *after* the product was marketed. Because of the new technique developed with this product, Ethicon

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[269] ETH-00255 - 00256
[270] ETH-00264
[271] ETH-48130
[272] ETH-85678 (Email from Dr. Butrick to David Robinson: "POP does not cause pain!!!")
[273] Kirkemo Deposition 4-18, p97-98
[274] ETH-85676 (Butrick to Robinson, "I sure am getting tired of seeing these pts with bad myofascial pain after Prolifts…")
[275] ETH-85678 (slide from Butrick, "The aggressive surgery flares the pre-existing myofascial pain…")
[276] ETH-00264
[277] ETH-07712
[278] ETH-48130
[279] ETH-65877-65884
[280] ETH-16986
[281] ETH-17061
[282] Hinoul Deposition 4-6, p408-410
[283] ETH.MESH.00095913

recommended advanced training for surgeons prior to performing the Prolift procedures.[284,285,286,287]

Surgeon selection criteria for advanced training was initially focused on highly-skilled and experienced surgeons. Despite their advanced skill level, many of the surgeons had to be re-trained shortly after Prolift's launch.[288]

Despite Ethicon being provided feedback regarding the inadequacy of the training/trainees for the Prolift procedures, Ethicon representatives pushed the envelope on training. Ethicon did not want a repeat of the transobturator stress urinary incontinence inter-company competition where Ethicon was in a catch-up position from launch.[289,290]

In marketing materials, Ethicon claimed that Prolift was appropriate for almost all patients but it had no clinical evidence to support these claims.[291,292]

Hydrodissection is a surgical step used to create a space between the vagina and the rectum and/or bladder. The purpose of this step is to identify and surgically enter the rectovaginal/vesicovaginal space more easily and to reduce the risk of injury to the adjacent rectum and/or bladder. This step would seem even more important given the differences between vaginal dissections in Prolift procedures versus traditional procedures. However, the Prolift IFU makes no mention of vaginal wall hydrodissection. The Surgical Guide merely lists hydrodissection as a bullet-point item "to be considered as optional."[293] However, from internal documents and feedback from surgeons, Ethicon understood the importance of hydrodissection to minimize complications for surgeons unfamiliar with the vaginal dissection required for the Prolift procedure. Subsequently, there were many surgeons unaware of the potential importance of this potential surgical step.[294,295,296,297,298,299,300,301,302,303,304,305]

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[284] *See* ETH-83318
[285] *See* ETH-62214
[286] *See* ETH-83323
[287] *See* ETH-01624
[288] ETH-62214 (Email from Vie [Education Development Manager] dated 5-17-2005: "…16 of the 84 [surgeons trained as of May 3] have needed to be retrained (19%)…")
[289] ETH-83193 – 83194 (email from Miller [proctor] dated 12-10-2005 regarding preceptorship: "…I thought a couple of those guys were going to poke somebody's eye out.")
[290] ETH-83318 (email from Sweatt [District Manager] dated 6-27-2006: "…The reps push the envelope on training because they don't want to see a repeat of the obturator wars, where we were in a catch up position from launch. Our current labs don't really discuss Gynemesh, which is what most doctors should in fact be using at this point.")
[291] ETH-00260
[292] ETH-00264
[293] ETH.MESH.00419573
[294] ETH-74435 ("key for minimizing erosion risk")
[295] ETH-02707-02708 ("…critical to maintaining low rates of mesh exposure seen by experienced…users.")
[296] ETH.MESH.PM.000019
[297] ETH.MESH.00419571-00419600
[298] ETH-20085
[299] ETH-60151 ("Hydrodissection is key in helping…")
[300] ETH.MESH.00158295 (Prolift Forums and Round Table Summary of experienced Prolift surgeons – "Hydrodissection was identified as a key procedural step")
[301] ETH-19943

Initially, Ethicon provided no guidance and subsequently provided inadequate guidance to surgeons as to the necessity of performing a cystoscopy (a procedure looking into the bladder at the time of Prolift Anterior and Prolift Total POP surgery).[306,307,308,309,310,311] Nor did Ethicon discuss the critically important issue of timing of the cystoscopy in conjunction with the Prolift procedures. A cystoscopy is an essential step following the blind passage of the Prolift. Guides/trocars to detect if there has been any inadvertent damage to the bladder. The surgeon can reassess the bladder following trocar removal to determine the most appropriate management for the patient, including cancelling the planned mesh insertion, as recommended by the Prolift surgical guide.[312,313] In the original Prolift IFU, there was no information regarding the need for cystoscopy or the appropriate timing of an intraoperative cystoscopy to detect potential bladder injury. Although the original draft version of the IFU did have a statement regarding intraoperative cystoscopy, the final version of the original IFU omitted such recommendation.[314,315]

Prolift surgeons recommended that cystoscopy be performed in all Prolift procedures.[316,317,318,319,320,321] However, Ethicon ignored this feedback and did not place this requirement in the IFU or the Surgical Guide.

Ethicon ignored a request by the FDA that cystoscopy be recommended. Instead, Ethicon added a statement in the Prolift IFU that cystoscopy was "optional."[322,323]

Ethicon understood that at many hospitals, surgeon credentialing for cystoscopy performance was limited by specialty, especially limiting gynecologists.[324] Thus, if cystoscopy were stated as a requirement in the Prolift IFU, surgeons without credentialing for cystoscopy (many gynecologists) would not be credentialed to perform Prolift surgery independently. So, in

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[302] ETH-08028
[303] ETH.MESH.00008084
[304] Robinson Deposition 3-13, p193-196
[305] Henderson Deposition p146
[306] ETH-02711
[307] ETH-80643
[308] ETH-19622
[309] ETH-19944
[310] ETH-02713
[311] ETH-19645
[312] ETH.MESH.00419571 – 00419600
[313] Hinoul Deposition 4-6, p609-610
[314] ETH-62799
[315] ETH-62803 - 62808
[316] ETH-02711
[317] ETH-80643
[318] ETH-19622
[319] ETH-19944
[320] ETH-02713
[321] ETH-19645
[322] ETH-01242 – 01248 (12-20-2007 Communication from FDA to Ethicon regarding the Prolift and Prolift-M 510K's requesting "Please add a warning…")
[323] ETH-01761 2-22-2008 response by Ethicon stating that they would revise to say that "Cystoscopy may be performed…")
[324] Henderson Deposition 10-5, p457

order to broaden their market to surgeons not credentialed in cystoscopy, Ethicon chose to only list cystoscopy as an option, at the expense of patient safety.

Reducing the size (trimming) of the Prolift mesh is recommended in the Guide.[325] However, there is no explanation given to the implanting surgeon as to the standardization of when trimming is "*required*," what constitutes "*small reductions*," nor what constitutes a "*proper fit*" of the anterior and posterior mesh implants. The Guide only states in one place that, *"[i]t is recommended to avoid large vaginal excisions…*"[326] No other guidance is given by Ethicon despite the fact that their consulting surgeons expressed to them how important it is to consider the anticipated amount of mesh contraction in determining whether and how much vaginal trimming to perform.[327,328]

The Prolift POP Procedure is not truly "*standardized*." The first sentence of the Prolift Guide claims that, *"[t]he objective of the Prolift procedure is to achieve a complete anatomic repair of the pelvic floor defects in a standardized way*." However, one of the most important concepts of the Prolift procedure is "*tension-free*" placement of the mesh implant, which cannot be standardized given both the patient-to-patient and the surgeon-to-surgeon variability in detecting this.[329]

Ethicon representatives acknowledge that there is no standardized means of determining whether Prolift mesh is in fact, "*tension-free*." After four years of selling and training the Prolift procedures, Ethicon still had problems training surgeons on standardizing the "tension-free" aspects of the procedure.[330,331,332]

It is generally accepted that the correct positioning and tensioning of the mesh and mesh arms is an essential surgical step to prevent needless complications. However, Ethicon provides no standardized instruction on how to ensure that this critical step is performed correctly. Ethicon documents describe fixation of Posterior Straps (Transgluteal or vaginal approach). Two perineal incisions bilaterally and the cannulas are passed through gluteal area to traverse the sacrospinous ligament and exit into the vaginal incision. Each of the two posterior straps is shortened and fixed directly to the sacrospinous ligament bilaterally.[333]

However, there is no guidance provided by Ethicon to the surgeons regarding: (a) how to decide whether sacrospinous fixation of the posterior straps is necessary or preferred over the transgluteal approach; (b) how to decide the proper length for trimming the posterior straps in a "standardized" manner; and (c) how to determine best means of affixing the shortened posterior straps to the sacrospinous ligaments in a "standardized" manner.

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[325] ETH.MESH.00419584 - 00419585
[326] ETH.MESH.00419572
[327] ETH-80641 ("Mesh will contract up to 30%.")
[328] Robinson Deposition 3-13, p260
[329] ETH.MESH.PM.000019
[330] ETH-49659
[331] Hinoul Deposition 4-5, p506-507
[332] Kirkemo Deposition 4-18, p135-135, p150
[333] ETH.MESH.00419582

Positioning of the anterior segment of the Prolift is intended to be placed under the bladder in lateral contact with the arcus tendineus fascia pelvis.[334,335] But, the Surgical Guide does not give any guidance on how to accomplish this in a standardized manner, raising a number of questions regarding technique to accomplish this step.

Positioning of the posterior segment of the Prolift is intended to be placed above the rectum in lateral contact with the superior surface of the levator ani muscles.[336 337 338 339] But, the Surgical Guide does not give any guidance on how to accomplish this in a standardized manner, raising a number of questions regarding technique to accomplish this step.

Adjusting the position and the tension of the Prolift is addressed in the Guide.[340] But it gives no guidance on how to determine: (1) when and whether "further adjustments of tension and position" will be neither necessary, nor (2) the magnitude of "further adjustments" in a "standardized" manner.[341 342] Again, in 2009, more than four years after the launch of Prolift, Ethicon was made aware of the difficulty in teaching "tension-free" placement in a "standardized" manner.[343] Since mesh arm tensioning and positioning are such an essential aspect to reducing complications, it is wholly unacceptable for such a critical surgical procedure to be left without clear instructions for the surgeon.

A surgeon would reasonably expect Ethicon's Surgical Guide to provide useful guidelines on critical maneuvers and measures to avoid needless complications. The absence of recommendations and potential complications would reasonably imply to a surgeon a lack of importance of key surgical steps. It is important to keep in mind that Ethicon developed and patented the TVM technique and surgical procedure, which was, according to Ethicon, a "major mind shift" in urogynecological surgery. At a minimum, Ethicon should have provided key technique guidelines, warnings, and recommendations based upon high volume surgeons' experience and feedback such as:

- Warnings regarding the increased risk of urinary incontinence following Prolift Anterior and Prolift Total repairs.
- Need for hydrodissection of vaginal wall.
- Critical role of permanent suture at base of cervix.
- Importance of proper vaginal wall dissection to prevent complications.
- Importance of mesh trimming and need for it to be done properly.
- The implications of performing a uterine preserving repair vs. hysterectomy vs. post-hysterectomy Prolift Total POP repair.

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[334] ETH.MESH.00419584
[335] ETH.MESH.PM.000019
[336] ETH.MESH.00419585
[337] ETH.MESH.PM.000019
[338] Hinoul Deposition 4-5, p506-507
[339] Kirkemo Deposition 4-18, p135-135, p150
[340] ETH.MESH.00419584 – 00419585
[341] Hinoul Deposition 4-5, p506-507
[342] Kirkemo Deposition 4-18, p135-135, p150
[343] ETH-49659 (email dated 8-10-2009 from Kirkemo: "A real misconception exists in the community…. We really need to think about how to change our teaching…")

- Recommendations to accurately pass the transobturator trocars blindly into the proper anatomic locations.
- Recommendations regarding the importance of feeding the mesh without twisting through the Prolift Cannula, resulting in preventable complications if this step is incorrectly performed
- Recommendations regarding the crucial importance of proper mesh tensioning, resulting in preventable complications if this step is incorrectly performed.
- Essential need for cystoscopy to rule out inadvertent bladder perforation.

Mesh exposure and bladder injury are common complications, yet there is inadequate guidance in the Surgical Guide on managing these complications. An absence of a description and guidance in the management of these complications minimizes the frequency and magnitude of these complications to a surgeon.

Dyspareunia, vaginal pain, and pelvic pain are common complications following Prolift POP procedures, yet there is inadequate information in the Surgical Guide explaining the lack of a safe and effective method to treat these complications. The absence of this information minimizes the frequency and magnitude of these complications to a surgeon.[344] [345]

IX. FALSE AND MISLEADING STATEMENTS BY ETHICON

A. Prolift mesh provides "*long-lasting stabilization of fascial structures of the pelvic floor in vaginal wall prolapse*".[346]

Clinicians reading this statement would reasonably assume that Ethicon possessed evidence from clinical trials that Prolift Pelvic Floor Repair System had demonstrated "long-lasting" effectiveness. However, Ethicon had no such evidence as of March 2005, when marketing of Prolift Pelvic Floor Repair System was initiated.[347,348,349] Ethicon still had no such evidence as of August 2007 to May 2008, when the FDA review of Prolift Pelvic Floor Repair System was ongoing. In September 2007, Ethicon informed the FDA that "no clinical investigations were conducted on the use of Prolift Pelvic Floor Repair System."[350] Therefore, Ethicon's use of the term "long-lasting" had no factual basis. By claiming that Prolift produces "stabilization of fascial structures of the pelvic floor in vaginal wall prolapse," Ethicon implies that studies had been performed to directly assess the anatomic and physiologic effect of the Prolift system on the pelvic floor. Clinicians reading such a statement would reasonably and incorrectly assume that studies had demonstrated a direct and beneficial effect of Prolift placement on fascial structures that provide pelvic floor support. However, Ethicon had no such evidence at the time marketing of Prolift was initiated in March 2005.

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[344] ETH.MESH.00419571 - ETH.MESH.00419600
[345] ETH.MESH.00067363
[346] ETH.MESH.02589071
[347] Walji Deposition p300, p457,
[348] Gauld Deposition rough 4-26, p200
[349] Hinoul Deposition 4-5, p200
[350] ETH-00929 - 00930

In January 2005, Ethicon's own internal Clinical Expert Report on Prolift stated, "... in vivo forces and exerted strains on pelvic floor repairs during the postoperative period are not known." [351] [352] [353] Years after the Prolift was launched, Ethicon scientists still continued to search for answers regarding the estimated pelvic forces and how to develop a mesh that would compensate those forces. Because the forces on pelvic floor repair were unknown, there would be no way of knowing whether Prolift Pelvic Floor Repair System adequately compensated such forces. Other internal Ethicon documents confirm their conclusion that a lack of knowledge of pelvic floor forces leads to patient complications and that Prolift mesh was not designed to compensate these forces.[354]

B. Prolift Mesh had *"bi-directional elastic property"*. [355]

The Gynemesh PS mesh used in the Prolift Pelvic Floor Repair System does not stretch significantly. This is a direct contradiction to the claim that the Gynemesh PS mesh used in Prolift has elasticity of any kind, bidirectional or otherwise. Indeed, Ethicon eventually deleted the claim of bidirectional elasticity from the Prolift Pelvic Floor Repair System IFU due to lack of evidence. [356]

By claiming that the Gynemesh PS mesh used in Prolift has bidirectional elasticity, Ethicon implied that studies have been performed to prove that Prolift possesses these elastic design characteristics when used for the surgical treatment of vaginal prolapse. Clinicians reading such a statement would reasonably and incorrectly assume studies had demonstrated adaptation of the mesh to the stresses normally encountered by the unique movement of the vagina. Clinicians would reasonably conclude that, by having elastic properties in two directions, the mesh would allow for expansion of the vagina, which normally occurs during sexual activity, permitting comfortable penile penetration and thrusting of vaginal intercourse. However, Ethicon could produce no such evidence, despite making the claim of bidirectional elastic property of its meshes since 1985 for Mersilene mesh, Prolene Soft mesh, and Gynemesh PS mesh.

Ethicon had no such evidence that Gynemesh PS mesh in Prolift Pelvic Floor Repair System had bidirectional elastic properties at the time the marketing of Prolift was initiated in March 2005. Ethicon had no such evidence that Gynemesh PS mesh in Prolift had bidirectional elastic properties between August 2007 and May 2008, when the FDA review of Prolift was ongoing.[357] [358] [359] [360]

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[351] ETH-07156
[352] ETH.MESH.05237872 Mesh Properties – How important are they?
[353] ETH.MESH02227224 Thunder MGPP decision meeting
[354] ETH.MESH.02185584 Biomechanical Considerations for Pelvic Mesh Design; ETH.MESH.03753245 BIOMECHANICS
[355] ETH-00002
[356] ETH-00943
[357] ETH.MESH.00922443 - 00922445
[358] ETH.MESH.00869985
[359] ETH.MESH.00869987
[360] ETH.MESH.02589077 - 02589078

The FDA requested that Ethicon either remove the statement or provide evidence to support it.[361] On September 20, 2007, Ethicon admitted that they had no evidence to support the claim that the Gynemesh PS mesh in Prolift had bidirectional elastic properties. [362,363, 364] Nevertheless, the baseless claim that Gynemesh PS mesh in Prolift Pelvic Floor Repair System had bidirectional elastic properties remained in the Prolift IFU until 2009.

One of the inventors of the TVM technique as well as a number of other leading scientists and surgeons have attempted to determine the mesh requirements necessary to account for the unique nature of the variability in pelvic and vaginal tissues in terms of elasticity, stretchability, and anisotropy and have been unsuccessful in their studies to adequately define and characterize these parameters in order to define the material characteristics that would properly mimic the pelvic floor environment.[365 366]

C. Prolift Mesh *"remains soft and pliable".*

Ethicon's claim that the Gynemesh PS mesh used in Prolift Pelvic Floor Repair System remains soft and pliable postoperatively implies that studies have been performed to document this mesh characteristic when used for the surgical treatment of vaginal wall prolapse. [367 368 369 370 371] Clinicians reading such a statement would reasonably and incorrectly assume studies had been performed, which demonstrated the softness and pliability of the mesh after its placement in the vagina. Clinicians would reasonably conclude that mesh characteristics of softness and pliability would not interfere with sexual function after Prolift placement. However, Ethicon was well aware that mesh contraction occurred to some extent in all cases after Prolift placement. In many cases, mesh contraction occurred to the extent of causing complications, including chronic pain, pain with mesh palpation, vaginal rigidity, and dyspareunia. Ethicon was well aware of mesh contraction because of its experience with Prolene mesh and Prolene Soft mesh used for hernia repair. [372]

In addition, Ethicon had no evidence to support the claim that the Prolift "mesh remains soft and pliable" when used for the surgical treatment of vaginal wall prolapse. Indeed, Ethicon had evidence that directly contradicted the claim that the "mesh remains soft and pliable" from

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[361] ETH-00943
[362] ETH.MESH.00922443 - 00922445
[363] ETH-00938
[364] ETH.MESH.09656632
[365] Gabriel B, Rubod C, Brieu M, Dedet B, de Landsheere L, Delmas V, Cosson M. Vagina, abdominal skin, and aponeurosis: do they have similar biomechanical properties? Int Urogynecol J. 2011 Jan;22(1):23-7. Epub 2010 Aug 27.)
[366] Cosson M, Lambaudie E, Boukerrou M, Lobry P, Crépin G, Ego A. A biomechanical study of the strength of vaginal tissues. Results on 16 post-menopausal patients presenting with genital prolapse. Eur J Obstet Gynecol Reprod Biol. 2004 Feb 10;112(2):201-5
[367] ETH.MESH.00067357 (Lucente Webinar: "... the things that we all worried about tissue healing and comfort; the 2 things that, again, have plagued us all along using an implant, erosion and discomfort...")
[368] Walji Deposition p471-472
[369] Robinson Deposition 3-14 p683-684
[370] Kirkemo Deposition 4-18, p246-249
[371] Ciarrocca Deposition 3-29, p264-266
[372] ETH-80646

several sources, including physician experts, [373] internal documents related to Prolift + M (known as "Project Lightning") development, [374] and Ethicon-supported animal [375] and clinical studies. [376] Ethicon's French Medical Director, Axel Arnaud, stated that the mesh remaining "soft and pliable" after implantation was "an illusion."[377]

As of these key time periods (2005, 2007), there was abundant evidence in the scientific literature regarding mesh rigidity, contraction, shrinkage, fibrosis due to mesh foreign body reaction leading to lack of tissue in-growth, lack of vascularization, and scar plate formation. The origin of synthetic mesh contraction in the human body and in animal models has definitely shown that no mesh is inert. [378,379,380,381,382,383] This inflammatory reaction causes free radical synthesis, which then causes oxidation and degradation of polypropylene meshes.

Mesh degradation then causes more inflammation and, subsequently, more mesh contraction. When mesh contraction occurs in the abdominal wall or thoracic wall, it causes multiple conditions such as chronic pain, fibrosis, and infection. Similarly, when synthetic meshes are placed in the vagina for POP procedures, mesh responds the same way. When vaginal mesh contracts, it causes vaginal fibrosis, infection, chronic vaginal pain, chronic pelvic pain, vaginal shortening, vaginal narrowing, vaginal extrusion, adjacent organ erosion and dyspareunia.

D. *"Wound healing is not noticeably impaired"* by Prolift Mesh.

Similar to the Ethicon's claim regarding the softness and pliability of its mesh, it appears that Ethicon lacked evidence regarding wound healing following the surgical implantation of Prolift. As with noted above, in September 2007, Ethicon informed the FDA that "no clinical investigations were conducted on the use of Prolift Pelvic Floor Repair System". [384] However, there existed abundant evidence in the scientific literature regarding rigidity, contraction, shrinkage, fibrosis due to mesh foreign body reaction leading to lack of tissue in-growth, lack of vascularization, and scar plate formation. Ethicon's internal documents have meeting minutes from meetings between Ethicon representatives and their key outside consulting experts wherein the concept of a "chronic wound" that is created around the mesh was discussed. [385] Ethicon was told that the mesh continues to react in the tissues decades after implantation. So for Ethicon to claim that "wound healing is not noticeably impaired" is absolutely false and misleading given the information they had available to them both before and after the launch of Prolift.

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[373] ETH-82320
[374] ETH-77061
[375] ETH-60555 – 60556
[376] ETH-77061
[377] Arnaud depo 11/15/12 68:18-69:13
[378] ETH-80641 ("Mesh will contract up to 30%")
[379] ETH-80645 – 80651
[380] Hinoul Deposition 4-5, p 132-134, p147-149
[381] Kirkemo Deposition 4-18, p138, p151-152
[382] Robinson Deposition 3-13, p260
[383] Walji Deposition p465
[384] ETH-00929 - 00930
[385] ETH.MESH.00870466

E. The Prolift procedure is *"minimally invasive".*

As noted above, Ethicon claimed in its patient brochures that the Prolift procedure was a new and revolutionary minimally invasive procedure. This was inaccurate, and downplayed the invasive nature of the implantation surgery for the Prolift. In fact, Ethicon's own medical directors described the surgery as a major invasive procedure, yet Ethicon failed to timely correct its labeling. Ethicon's characterization of the Prolift procedure as minimally invasive is flat wrong, and no doubt falsely reassured doctors and patients.

F. Prolift Mesh is not *"subject to degradation".*

Ethicon states that the mesh contained in the Prolift System is not "*subject to degradation or weakening by the action of tissue enzymes.*"[386] [387] [388] There is scientific literature, however, which states just the opposite – polypropylene is not biologically inert and is, in fact, subject to oxidation and degradation. In fact, as stated above in this report, Ethicon's own internal studies and a significant amount of readily available medical literature specifically concludes that polypropylene mesh incites a specific immune response, creating within the vagina a foreign body reaction that directly causes mesh degradation, mesh contraction, fibrosis, vaginal narrowing, pelvic pain, and dyspareunia. [389] [390] [391]

Despite its own internal studies and numerous peer-reviewed articles regarding degradation, Ethicon failed to change its IFU, its surgical guide, its patient brochures, or its marketing materials to acknowledge that degradation of the polypropylene in the woman's pelvic tissues not only would occur but that it would occur at varying degrees over the life of the implant.

G. Prolift Pelvic Floor Repair Systems *"restore normal sexual function"*

Ethicon admits it has no evidence to support claims regarding sexual function after implantation of the Prolift Pelvic Floor Repair Systems.[392] [393] [394] [395] [396] [397] [398] Nevertheless, at the

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[386] ETH-01777
[387] ETH.MESH.00570955
[388] ETH.MESH.02589066 - 02589068
[389] Walji Deposition 3-9 p399, p404, p457
[390] Gauld Deposition rough 4-26, p200
[391] Hinoul Deposition 4-5, p200, Hinoul Deposition 4-5, p 132-134, p147-149, Kirkemo Deposition 4-18, p138, p151-152, Robinson Deposition 3-13, p260, Liebert T, Chartoff R, Costgrove S. Subcutaneous Implants of Polypropylene Filaments. J.Biomed. Mater. Res. 1976; 10:939-951, Williams D. Review Biodegradation of surgical polymers. Journal of Materials Science. 1982; 17:1233-1246, Celine Mary, Yves Marois, Martin W. King, Gaetan Laroche, Yvan Douville, Louisette Martin, Robert Guidoin, Comparison of the In Vivo Behaviour of Polyvinylidene Fluoride and Polypropylene Sutures Used in Vascular Surgery, ASAIO Journal, 44 (1998) 199-206, Wood, et al. Materials Characterization and histological analysis of explanted polypropylene, PTFE, and PET hernia meshes from an individual patient. J Mater Sci: Mater med (2013) 24:1113-1122, DEPO.ETH.MESH.00000367, ETH.MESH.09557798, ETH.MESH.15144988, ETH.MESH.00874032, ETH.MESH.07192929, B. Klosterhalfen presentation "What can we learn from explanted meshes?", Depositions of Thomas Barbolt and Daniel Burkley and exhibits thereto
[392] ETH-48281: email from Scott Jones 3-5-2009 "... Apparently, Bos Sci [Boston Scientific] has been talking to doctors about the 'banding' effect that occurs with the anterior Prolift.... The banding that customers are telling me occurs at the edge of the mesh near the apex. Regardless of how doctors adjust the mesh, there is still a definite ridge or banding that can be vaginally palpated with our anterior mesh. In fact, during my discussions with Dr. Raul

same time, Ethicon claims in its Patient Information Brochure, "[*The Prolift Pelvic Floor Repair Systems] allows for the restoration of sexual function by restoring vaginal anatomy.*" In fact, as of June 2006, the opposite was shown in a study that demonstrated the number of sexually active patients decreased from 61/90, (68%) at baseline, to 42/90, (47%) at 6 months, and to 40/90, (44%) at 12 months. One-third of patients who were sexually active before surgery became sexually inactive after mesh surgery. The substantial reduction in the number of sexually active patients strongly suggests that many patients abandoned attempts at sexual activity due to dyspareunia or other complications of mesh surgery. Also, it is critical to note that all results described are short term (less than two years). [399]

As is reported in the literature and as I have seen in my own clinical practice, mesh-specific complications, such as mesh contraction leading to dyspareunia, can be delayed many years following implantation. Therefore, the true frequency of dyspareunia is greatly underestimated. Evidence shows that Ethicon had knowledge of impaired sexual function and dyspareunia, but rather than disclosing this knowledge, Ethicon intentionally chose to not disclose the evidence they had in their possession regarding the full extent of complications of sexual dysfunction. [400] [401] [402] [403] [404] [405]

X. ETHICON'S INSTRUCTIONS FOR USE (IFU) AND KNOWN RISKS RELATED TO THE PROLIFT WERE NOT DISCLOSED

At the time of the Prolift launch, Ethicon was fully aware of all the risks associated with the Prolift product. Ethicon did not fully or adequately disclose the risks, adverse reactions, or the clinical consequences thereof in the Prolift Instructions for Use (IFU) despite Ethicon's internal awareness of these risks (as demonstrated by extensive internal documentation, ETH.MESH.06372356-ETH.MESH.06372363; ETH.MESH.02026591-02026595) and the deposition testimony of its employees:

Mendelovici yesterday, he told me that he is so frustrated with the banding effect on the anterior Prolift that he is now modifying his mesh to provide better anterior apical support, and to reduce banding (different modification than Raders or Lucente)... this banding has not been clinically significant for most patients, but the impression in the surgeons eyes is that this is unacceptable, and they will try to avoid this if possible.... ")

[393] ETH-71307 (3 of 14 patients with unresolved symptoms with palpable mesh banding)

[394] ETH-02689 ("surgical release of mesh banding" was necessary for patients with persistent dyspareunia)

[395] ETH-82419 (Summary of meeting points Sexual function June 2006: "Previous history says that we want to avoid this discussion without a solid case for Prolift....")

[396] ETH-01121 June 2006 "...New onset dyspareunia was reported in 7 patients [of 61 patients] at 6 months and in 3 patients at 12 months

[397] ETH-48769 (Email 5-9-2009 addressing Pinnacle competition "...remember that de novo dyspareunia is a post op safety concern")

[398] ETH.MESH.00067357 (Lucente Webinar: "... the things that we all worried about tissue healing and comfort; the 2 things that, again, have plagued us all along using an implant, erosion and discomfort...")

[399] ETH-01121

[400] ETH-80645 - ETH-80651

[401] ETH.MESH.00067363

[402] Walji Deposition 3-8, p398-399, p457

[403] Gauld Deposition rough 4-26, p200

[404] Hinoul Deposition 4-5, p200

[405] Robinson Deposition 3-13 p299

1. Dr. Martin Weisberg
2. Dr. Piet Hinoul,
3. Dr. David Robinson,
4. Dr. Axel Arnaud,
5. Mr. Joerg Holste,
6. Dr. Aaron Kirkemo
7. Jennifer Paine
8. Catherine Beath
9. Ms. Zenobia Walji,
10. Ms. Judy Gauld
11. Dr. Aran Maree
12. Mr. Daniel Smith
13. Mr. Sean O'Bryan
14. Dr. Charlotte Owens
15. Mr. Scott Ciarrocca
16. Dr. James Hart
17. Bryan Lisa
18. Brian Kanerviko
19. Price St. Hilaire
20. Paul Parisi
21. Alex Gorsky
22. Renee Selman
23. Cliff Volpe

Each of the risks, adverse reactions, contraindications, and warnings, and the clinical consequences, should have been clearly placed and stated in the IFU so that the patients' implanting surgeon would be fully informed, and so the patient could have been informed. The following lists inadequacies in the development of the Prolift and the information provided to physicians and patients:

1. Inadequate pre-launch testing and durability studies.
2. Ineffective procedure puts women through extensive surgery with unacceptably high failure rate.
3. Dangerous procedure with incomplete IFU specifications regarding tensioning and appropriate use of trocars thereby leading to complications and failure.
4. Inadequate data to support use of Prolene Soft polypropylene mesh through the Prolift procedure in the Pelvic Floor.

5. Failure to disclose that Prolift complications are not able to be safely and effectively treated in certain patients, including the inability to safely and effectively remove the mesh when necessary, and that the complications can result in chronic, permanent debilitating pain.

6. Inaccurate and misleading claim in the IFU that the inflammatory response is slight and transient, whereas Ethicon has admitted it is chronic and in some patients severe.

7. Incomplete warnings regarding the inherent nature of the polypropylene mesh, and that a predictable increased immune response to the presence of the mesh is set off, with an increased risk of product breakdown and failure.

8. Incomplete warnings regarding the significant risks for young and sexually active women, including the failure to include a warning written by Dr. Axel Arnaud for inclusion in the initial IFU because the project leader did not want to take the time or expense to reprint the IFU, and the failure to only indicate the procedure for severe prolapse of at least stage 3 or 4, where the alternatives would not be safe or feasible, consistent with internal documents and the writings of the French inventors of the procedure. In fact, Dr. Hinoul's report in 2012 regarding the procedure indicates that the Prolift is not indicated for a patient who does not fit the criteria to be an appropriate candidate.

9. That Prolift mesh causes a lifelong risk of vaginal erosion/extrusion.

10. That Prolift mesh causes a lifelong risk of pelvic organ erosion.

11. That erosions and extrusions will be severe and incurable in some women.

12. Incomplete warning and pre-launch evaluations regarding the host's acute inflammatory response to Prolift mesh.

13. That the polypropylene mesh used to manufacture Prolift contracts in all patients, and that in some patients, this leads to complications including but not limited to nerve entrapment, pain, chronic pain, recurrence of prolapse, vaginal wall stiffness, vaginal anatomic distortion, erosion, and when this occurs the mesh cannot be safely and effectively revised or removed as necessary, including the body of the implant, and the deep arms which are virtually impossible to safely and effectively treat.

14. Incomplete warning and pre-launch evaluations regarding the risks and consequences of the host's chronic inflammatory response to Prolift polypropylene mesh.

15. That the Prolift mesh pore size is inadequate, especially in actual use, and as a result of tension and strain both during and following implantation causes fibrotic bridging/scar plating and increased contraction, and the consequences thereof.

16. That the polypropylene resins used in the meshes in Prolift have been associated with causing sarcomas at the implantation site.

17. Insufficient evaluation regarding implantation of the Prolift product into the contaminated field of the vagina.

18. Insufficient evaluation regarding Prolift product degradation/product failure due to product degradation.

19. Insufficient evaluation and warnings regarding polypropylene-related complications not seen in traditional repair.

20. Insufficient evaluation regarding and warning regarding long-term hypersensitivity to polypropylene mesh.

21. That Ethicon knew of data that the risk and consequences of vaginal scarring was greater than it disclosed in its IFU.

It is my opinion to a reasonable degree of medical probability that the Prolift is defective due to Ethicon's failure to adequately design and test the product prior to launch, failure to properly evaluate and act in response to adverse event reports and informal communications from surgeons notifying Ethicon of catastrophic complications and the failure to appropriately warn patients and health care providers of the range, severity and magnitude of the risks and complications, and consequences thereof, including, but not limited to, the following:

a. The mesh will degrade, fragment, and elongate in some patients;

b. The risk of chronic, refractory infections resulting from the fact that the mesh will potentiate infection (contrary to the professional education and marketing documents);

c. The complications and consequences due to the chronic foreign body reaction due to the presence of the product;

d. The risk of permanent vaginal or pelvic scarring as a result of the interaction with the host;

e. The risk and consequences of vaginal extrusion;

f. The risk of permanent vaginal shortening as a result of the product;

g. The risk of intractable pelvic, vaginal, urethral, and systemic pain resulting from the product's interaction with the body;

h. The need for corrective or revision surgery to revise or attempt to remove the product, which cannot be safely or effectively achieved in many instances;

i. The severity of complications such as pelvic pain, vaginal pain, dyspareunia, overactive bladder, urinary retention and other symptoms and conditions, voiding pain that could arise as a result of implantation of the product;

j. That the Prolift causes permanent mesh based dyspareunia;

k. That the Prolift causes permanent pelvic pain;

l. That the Prolift causes narrowing of the vaginal vault.

m. The frequency of complications that result from implantation of the product;

n. Folding, wrinkling, and bunching of the mesh inside the body, increasing the risk of contraction and other complications;

o. Treatment of pelvic organ prolapse is no more effective than feasible available alternatives such as colporrhaphy;

p. Treatment of pelvic organ prolapse with the Prolift procedure exposes patients to greater, and medically unreasonable risks than feasible available alternative procedures;

q. Treatment of pelvic organ prolapse with the Prolift makes future surgical repair more difficult than the feasible available alternative procedures;

r. The use of the Prolift procedure puts the patients at greater risk of requiring additional and morbid surgery;

s. The removal of the products due to complications may involve multiple surgeries, significantly impair the patient's quality of life, and ultimately not successfully treat the condition;

t. Complete removal of the products is most likely not possible and may not result in resolution of the complications, including but not limited to pain, contraction and scarring and recurrent urinary leakage and pelvic organ prolapse;

u. Insufficient evaluation regarding and warning regarding the pullout forces of the polypropylene arms;

v. Insufficient evaluation regarding and warning regarding the pullout forces of polypropylene arms if the mesh were to be adjusted (pulled back and forth) during the mesh tensioning portion of the procedure;

w. Insufficient evaluation regarding and warning regarding the mesh anchoring configuration and "rolling potential" once in place in the body and muscle and fascia;

x. Insufficient evaluation regarding, warning and IFU guidance for, polypropylene mesh placement in morbidly obese patients.

It is my opinion to a reasonable degree of medical probability that Ethicon did not fully disclose the above risks and those discussed in this report, in its IFU and to surgeons and thereby denied the patient the right to full information about her surgery. This is true despite the information being readily available and known to Ethicon about these risks, which predate the launch of the device

XI. Statement of Opinions

My opinions are based on my personal knowledge, experience, and my investigation in this case. All of my opinions, and the basis of these opinions, are true and correct to the best of my knowledge and belief, including those related to scientific and medical issues, which I believe are true and correct to a reasonable degree of scientific and medical probability.

A. Lack of Clinical Benefit:

1. Patients implanted with non-absorbable, transvaginal synthetic mesh for pelvic organ prolapse, including Prolift Pelvic Floor System, do not have improvement in symptomatic results over traditional, non-mesh repair.

2. Patients implanted with non-absorbable, transvaginal synthetic mesh for pelvic organ prolapse, including Prolift Pelvic Floor System, do not have improvement in or quality of life (QOL) over traditional, non-mesh repair.

3. Patients implanted with non-absorbable, transvaginal synthetic mesh for pelvic organ prolapse, including Prolift Pelvic Floor System, do not have improvement reoperation rate over traditional, non-mesh repair.

4. Because of the lack of benefit of Prolift Pelvic Floor System, the increased patient risks, complications, and added expense of these products far outweigh any stated or implied benefit.

5. There was no need for Prolift Pelvic Floor System, a non-absorbable, synthetic mesh, to be sold and marketed as a surgical treatment and procedure for pelvic organ prolapse (POP) as there were safe, effective and reasonable alternative surgical treatments available at the time this product was launched that did not needlessly endanger patients nor carry the likelihood or risk of serious injury that the Prolift product did.

B. Complication Rate:

1. Synthetic transvaginal meshes for POP, including Prolift Pelvic Floor System, subject patients to needless danger through increased risks not present in traditional, non-mesh surgery for POP repair. Prolift has, therefore, caused serious and potentially permanent injuries due to complications associated with its implantation for POP repair.

2. Based on the information that was easily and readily available and abundant in the scientific literature, as well as the information known by Ethicon at the time it launched Prolift Pelvic Floor Repair Systems in 2005, a reasonably prudent and publicly responsible manufacturer should have never put this product on the market knowing that it would be permanently implanted into the pelvic region of female patients.

3. Even when surgeons used the Prolift Pelvic Floor Repair Systems as designed and marketed, it was unsafe to patients for its intended use as a method of surgical POP repair because of patient-to-patient anatomic variability and surgeon-to-surgeon variability in experience, training and technique.

4. Because non-absorbable, synthetic, polypropylene mesh such as Prolift causes an intense foreign body reaction in pelvic tissue, there is no way to safely implant these products into a woman's pelvic tissue without an increased risk of serious complications including, but not limited to, pain associated with the implant procedure (nerve and tissue damage), chronic pelvic pain associated with fibrosis and scarring, chronic infection associated with, among other things, the product's implantation into a clean/contaminated field and the intense inflammatory response to the polypropylene, chronic wound healing issues, organ erosion, vaginal extrusion/exposure, chronic pelvic pain associated with the explant procedure (nerve and tissue damage) , de novo incontinence, and significant dyspareunia (painful intercourse).

C. Data Withheld From Physicians:

1. Ethicon, the manufacturer of Prolift Pelvic Floor Repair Systems, knowingly failed to completely disclose the known risks of prolapse surgery using Prolift to physicians and patients. By withholding this information and failing to provide adequate warnings and/or instructions, Ethicon failed to act as a reasonably prudent manufacturer, and knowingly exposed patients to needless, preventable danger, harm and permanent suffering.

2. Ethicon failed to disclose the lack of benefit of POP surgery using Prolift Pelvic Floor Repair Systems to physicians and patients. By withholding this information and failing to provide adequate warnings and/or instructions, Ethicon knowingly failed to act as a reasonably prudent manufacturer and thereby exposed patients to needless danger and harm.

3. For reasons that only served to harm women and lure physicians into a false belief that Prolift Pelvic Floor Repair Systems only helped to improve sexual activity, Ethicon elected to not disclose the increased risks to sexually active women, and not to include a statement regarding the possibility of Prolift POP surgery to cause "pain with intercourse and pelvic pain", and as a result, countless women were,

and will be, permanently and needlessly forced to suffer lifelong pain and embarrassment in part due to this decision to withhold essential information.

D. Breach of Duty by Ethicon:

1. Ethicon breached its duty of reasonable care to implanting surgeons and to patients by marketing and selling Prolift Pelvic Floor Repair Systems as a new surgical device *and* procedure with insufficient evidence of either the product's or the procedure's safety, effectiveness and benefit despite knowing the risks of non-absorbable, synthetic surgical mesh for POP, including its product, Prolift.

2. Ethicon breached its duty of reasonable care to implanting surgeons and to patients by marketing and selling Prolift Pelvic Floor Repair Systems (both the product *and* the procedure) to surgeons and patients without proper warnings, without proper instructions for use and without sufficient evidence of its safety and efficacy, thereby exposing them to needless danger and unreasonable risk of harm.

3. Ethicon breached its duty of reasonable care to implanting surgeons and to patients by failing to disclose its knowledge of a significant increase in complications associated with Prolift through physician communications, "Dear Surgeon" letters, its sales force, sales and marketing brochures to physicians and patients and/or updates to its Instructions for Use to physicians.

4. Ethicon breached its duty of reasonable care by knowingly and falsely marketing Gynemesh PS to physicians as if the product was specially designed for treatment of POP while its intended and documented design was for abdominal wall hernia and "other fascial defects."

XII. PREVIOUS TESTIMONY

On November 21, 2015, my trial deposition testimony was given in *Patricia L. Hammons v. Ethicon, Inc., et al.;*. All of my opinions and testimony contained within that transcript are incorporated herein by reference and attached as Exhibit "C". Additionally, as noted in Section XI below, I have given testimony and provided expert reports in numerous Ethicon transvaginal mesh cases over the past few years. All of my testimony and opinions therein are hereby incorporated by reference.

I reserve the right to modify these opinions as necessary based upon any new or additional information or data that I may obtain or with which I am presented including, without limitation, any materials that I produce in response to Ethicon's requests.

XIII. EXHIBITS

Exhibit "A" contains a copy of my current Curriculum Vitae.

All materials that have been available to me to consider in support of my finding and opinions are included above and listed below in Exhibit "B".

November 21, 2015 Bene Esse Transcript attached as Exhibit "C"

Patricia L. Hammons v. Ethicon, Inc., et al.; Philadelphia County Court of Common Please Case No. 0003913 – Report attached as Exhibit "D"

Linda Gross et al. v. Gynecare, et al.; Superior Court of New Jersey Law Division – Middlesex County Case No. MID-L-9131-08– Reports attached as Exhibit "E"

Linda Gross et al. v. Gynecare, et al.; Superior Court of New Jersey Law Division – Middlesex County Case No. MID-L-9131-08– Deposition attached as Exhibit "F"

Diane Bellew v. Ethicon et al.; United States District Court, Southern District of West Virginia Case No. 2:12-cv-22473 – Reports attached as Exhibit "G"

Diane Bellew v. Ethicon et al.; United States District Court, Southern District of West Virginia Case No. 2:12-cv-22473 –Deposition attached as Exhibit "H"

Diane Bellew v. Ethicon et al.; United States District Court, Southern District of West Virginia Case No. 2:12-cv-22473 –Trial testimony attached as Exhibit "I"

Dale Watkins et al. vs. Ethicon, Inc. et al.; Superior Court of New Jersey Law Division – Bergen County Case No. BER-L-13787-14 MCL – Report attached as Exhibit "J"

Dale Watkins et al. vs. Ethicon, Inc. et al.; Superior Court of New Jersey Law Division – Bergen County Case No. BER-L-13787-14 MCL –Deposition attached as Exhibit "K"

Mullins et al v. Ethicon, Inc., et al.; Southern District of West Virginia Charleston Division Case No. 2:12-cv-02952 – Report attached as Exhibit "L"

Mullins et al v. Ethicon, Inc., et al.; Southern District of West Virginia Charleston Division Case No. 2:12-cv-02952 – Deposition attached as Exhibit "M"

Powerpoint Presentation used during Hammons de bene esse testimony attached as Exhibit "N"

XIV. RECENT TESTIMONY

Coloplast A/S v. Generical Medical Devices; United States District Court – Western District of Washington at Tacoma Case No. C10-227BHS

Linda Gross et al. v. Gynecare, et al.; Superior Court of New Jersey Law Division – Middlesex County Case No. MID-L-9131-08– Report & Deposition

Diane Bellew v. Ethicon et al.; United States District Court, Southern District of West Virginia Case No. 2:12-cv-22473 – Report, Deposition & Trial

Janice L. St. Cyr v. C.R. Bard, Inc. et al.; United States District Court, Southern District of West Virginia Case No. 2:14-cv-02313

Kathleen Stanbrough v. C.R. Bard, Inc. et al.; United States District Court, Southern District of West Virginia Case No. 2:14-cv-06937

Sheila Sutton v. C.R. Bard, Inc. et al.; United States District Court, Southern District of West Virginia Case No. 2:14-cv-00105

Pamela Ailey v Cook Medical, Inc., et al.; United States District Court, Southern District of West Virginia Case No. 2:13-CV-20496

Patricia L. Hammons v. Ethicon, Inc., et al.; Philadelphia County Court of Common Please Case No. 0003913 – Report & De Bene Esse

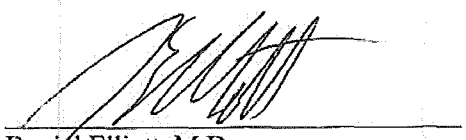
Dale Watkins et al. vs. Ethicon, Inc. et al.; Superior Court of New Jersey Law Division – Bergen County Case No. BER-L-13787-14 MCL – Report & Deposition

Mullins et al v. Ethicon, Inc., et al.; Southern District of West Virginia Charleston Division Case No. 2:12-cv-02952 – Report & Deposition

XV. COMPENSATION

I am compensated for investigation, study and consultation in the case at the rate of $700.00 per hour.

DATE:



Daniel Elliott, M.D